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ABSTRACT

This book is the first curriculum developed to bring cutting edge research on the HIV virus into science classrooms. The book and video are coordinated to provide a range of learning opportunities--labs, activities, readings, model design, guided discussions and, in the video, a way to see research in action. Both the book and video emphasize the human side of HIV--the focus of researchers, the work of clinicians, the battles fought by HIV-infected people--to make the science behind this infection real for students. Fundamental areas of biology and health education covered include cell biology, general virus and HIV structure, immune system function and HIV infection, the latest drug therapeutics, and infection prevention. This curriculum integrates the science of HIV with prevention education, can expand upon a biology or health curriculum, includes reproducible student activity pages with illustrations and electron micrographs, gives teachers background information and presentation strategies, presents current information on HIV diagnostic tests and therapeutic drugs, and examines the global impact of the AIDS pandemic. The video features animations of the complex concepts contained within the book, interviews with leading scientists and health care workers, compelling stories of adolescents living with HIV, and prevention strategies. (JRH)

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The Science of HIV

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The Science of HIV

by Michael DiSpezio

The Science of HIV *book and video were developed with funding from Abbott Laboratories and published by the National Science Teachers Association.*

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Electron micrograph p. 95, HIV-infected T cells, courtesy of National Institute of Allergy and Infectious Diseases, National Institutes of Health, Bethesda, Maryland.

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Graphs on p. 165 drawn using data from UNAIDS (Joint United Nations Programme on HIV/AIDS) of the World Health Organization.

HIV infections worldwide p. 166, drawn using data from "The Status and Trends of the Global HIV/AIDS Pandemic Symposium Final Report, Vancouver, 5–6 July 1996." AIDSCAP/Family Health International, Harvard School of Public Health, and UNAIDS (1996).

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North Falmouth, Massachusetts

The Science of HIV was produced by NSTA: Gerald Wheeler (Executive Director); Phyllis Marcuccio (Associate Executive Director for Publications); Shirley Watt Ireton (Special Publications Managing Editor); Doug Messier and Chris Findlay (Associate Editors); Jocelyn Lofstrom (Assistant Editor); Michelle Eugeni (Assistant Editor); and Christina Frasch (Editorial Assistant). Jocelyn Lofstrom was NSTA's project editor for *The Science of HIV*. Medical illustrations were created by Darryl Leja (Gaithersburg, Maryland). The line drawings were created by Martha Blalock (Silver Spring, Maryland). The book cover and design were created by Dianne Cook Burbank at Graves Fowler Associates, Inc. *The Science of HIV* was printed by Automated Graphic Systems.

Preface

Abbott Laboratories

More than a century ago, 30-year-old Wallace C. Abbott, M.D., began making a new form of medicine. Using the active part of medicinal plants, he formed tiny pills which provided a precisely measured amount of medicine. Within two years, the demand for these new pills exceeded the needs of Dr. Abbott's practice—and led to the incorporation of one of America's early pharmaceutical research companies.

Research at Abbott Laboratories today tackles the tough health care problems—including AIDS. Abbott's ELISA test was the first test to screen blood and blood products for the Human Immunodeficiency Virus (HIV), a key step in limiting the AIDS pandemic. Abbott research also has developed antibiotics specific to the infections that accompany the collapse of the immune system in AIDS and a nutritional supplement designed for AIDS patients. Abbott's *Norvir*, a protease inhibitor that blocks the production of an enzyme that HIV needs to reproduce, is extending the lives of people with HIV. But Abbott knows that, while research can answer the technical questions, education is the most effective weapon against HIV.

Abbott's education programs focus on the science behind the issues, offering a way to help students and the public understand the steps each must take to prevent and treat illness. For *The Science of HIV*, Abbott researchers and public outreach staff worked as a team with the National Science Teachers Association in the development of a curriculum that uses understanding of this virus as a cornerstone for contemporary biology education.

At the Museum of Science and Industry in Chicago, Abbott also has underwritten the first permanent U.S. museum exhibit on AIDS. This 4,000-square-foot exhibit provides accessible education on "AIDS: The War Within."

We must know everything about HIV before we can halt its spread and eliminate it. With knowledge, students can understand why they should avoid the behaviors that allow contagion. With knowledge, we can motivate young people to be the health professionals, technicians, statisticians, and researchers who will help find more effective treatments. *The Science of HIV* is designed to provide educators with background and teaching methods to effectively convey this knowledge.

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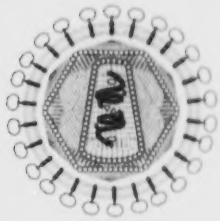

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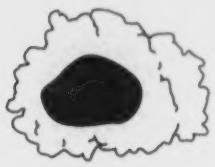

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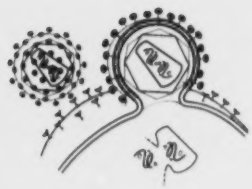

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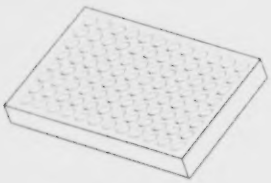

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Teacher Introduction

As teachers, we offer our expertise in hopes of improving the human condition. We guide students in their construction of essential thinking and decision making skills. When successful, our efforts help young people attain a productive, self-realized, and healthy life.

In the United States, the AIDS pandemic has raged for over a decade. Yet, ignorance and misconceptions about this virus abound. This lack of understanding may contribute to hundreds of thousands of new HIV infections in the coming years. As teachers, we should be concerned personally about preventing new infections; the AIDS pandemic will affect our own students—past, present, and future.

The Science of HIV has been created to fill a void in the classroom arsenal of teaching materials. Unlike other HIV/AIDS curricula, this package is geared towards the science classroom, to teach HIV using biological principles. It has been developed as both a stand-alone curriculum and as a source of extension activities to enhance a biology or health curriculum in middle school, high school, and some college classes.

How to Use this Book

If you have not been actively keeping up with news about HIV and AIDS, or you have never taught about HIV, you may be surprised at the amount of information in this book. The topic is quite detailed, and some of the information has only recently been reported.

This book contained current information at print time; but the field of HIV research is active and changes week by week. New information about HIV will be reported as you are teaching. Despite the grim nature of the AIDS pandemic, your students can benefit from the cutting-edge nature of HIV research. This highly visible, extensively reported-on field shows scientific research in action—make it a class project to keep up on the news during the school year. Perhaps have a bulletin board where new newspaper articles can be posted. Cheer on the scientists in the field as they develop new drugs and therapies and uncover more details about the nature of the virus. Some of these scientists, doctors, and health care workers are featured in the video (see below). For background, some helpful books, journals, and Internet sources are listed on pages 169–171.

The six chapters of the book are organized into sections. It's the instructor's choice whether to teach the book in order, as a full HIV/AIDS curriculum, or to just pick and choose sections. This offers each teacher the freedom to select the most effective presentation of subjects. Instructors may find that some sections are not appropriate for their classes; feel free to jump to the next, more suitable sections. Other classes, however, will find the logical and sequential development of concepts ideal for a section-by-section presentation.

The writer, editors, and reviewers of this book used the *National Science Education Standards* as a guide for inclusion of topics, for assessment methods, and for design of the teaching methods called for in the chapters. For example, the activities are designed to give students responsibility for extending their learning through experimentation, acquiring and interpreting information, and parallel problem solving. This project provides a vehicle for student inquiry into real questions that affect their lives and their futures.

Chapter Opening Pages

Each of the six chapters opens with a two-page spread. The right hand page can be reproduced for students to give a topic overview. A teacher summary is on the left hand page containing:

- **Curriculum Connections**—not a table of contents, but instead suggestions for where the topics in the chapter might fit into an existing biology or health curriculum. For example, parts of Chapter One could enhance teaching on eukaryotic cell structure and function.
- **Chapter Concepts**—a summary of the main points covered or what students will understand after completing the chapter.
- ***National Science Education Standards***—chapter concepts keyed to the National Science Education Content Standards to show where HIV education fits.

Student Pages/Teacher Pages

Each section has both student pages and teacher pages. Reproduce and hand out the student pages of sections you will teach. Line drawings and photographs have been selected and customized so that the image quality will not degrade substantially when photocopied.

In the student text, terms that are important or that may be unfamiliar are in **bold** the first time they appear. Vocabulary lists are only provided in the teacher sections to encourage students to ask questions, and also to allow teachers flexibility in using the vocabulary. For example, students could make their own concept maps using the vocabulary words.

Student sections are followed by teacher support pages. These pages include learning objectives, teaching tips, additional background information, answers to the student questions, and vocabulary definitions. These pages also identify the materials and preparations needed for the associated activities.

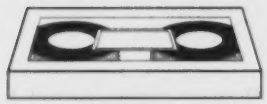
MARGIN BOXES

Margin boxes in both student and teacher pages are meant to give supporting or background information. Some margin boxes in the teacher pages give information on advanced topics or developing research that are not covered in student sections.

How to Use the Video

Unlike most teaching packages, this one comes with a dedicated video. The video, like the print material, addresses the science of HIV. The video will be broadcast on the Discovery™ channel. Because of television requirements, the video has two endings. Be sure to show your students the ending for the educational version of the video which appears after the credits.

This video should be used to motivate, deliver content, and assess learning. To motivate students, present this video in its entirety after the students have completed the introductory activity and have read the student introduction. When the video has ended, ask students to identify the familiar and unfamiliar concepts presented during the show. Challenge the class to compose a list of things they need to know in order to best understand all of the information presented in the video. Guide their inquiry to include concepts such as nucleic acids, viral replication, disease transmission, and HIV therapeutics. Post the completed list. As the concepts are covered during the school year, strike them from the list.



Video connections *suggest ways to connect the video to selected sections of the book. (Time indicated is measured from the start of the scene)*

While presenting sections that deal with cell function, immune response, HIV replication, DNA replication, and HIV therapeutic drugs, you may find it useful to replay the appropriate video clips. As these short animations are shown, use the pause button to freeze specific frames. Have students identify both the structures and actions that are occurring in the frozen frame. Encourage the students to compare and contrast the displayed animation with the actual event.

After the students have finished this book, present the video once more. This time it will be used as an alternate assessment tool. Have students review the list that was compiled when they first observed the show. After watching this repeat showing, challenge the students to fully describe each of the listed concepts.

Introductory Activity

As an introduction to this learning package, the following activity will give students a chance to think about HIV and AIDS without having much background. Don't tell students that the activity relates to HIV: It will become abundantly clear as they review their results. The student introduction to the book could follow up this activity to explain what they will learn about HIV in the coming weeks. A similar (but not the same) procedure in Chapter Four extends this activity to include epidemiology concepts—how to track the spread of disease.

Supply each student with a small plastic cup. In a class of 30 students, three of the cups should be filled one third with a dilute NaOH solution (made by dissolving 2 grams of NaOH into .5 liters of distilled water.)* The rest of the cups should be filled one third with water. Tell students that they have three rules. (1) They may share their liquids with as many or as few of their classmates as they like. (2) They must have liquid remaining in their cup after each exchange. (3) They have five minutes.

To do each exchange, instruct students to pour the contents of one cup into the other, swirl it gently, then return half the liquid to the other cup. When the five minutes are up and students are back in their seats, walk around the room adding several drops of phenolphthalein to each cup. Some of the samples will turn red when the indicator is added.

Suggest that the liquid within the cups represents their blood. Explain that some of the cups were infected with an unseen chemical that represents HIV. If their liquid remained clear after the indicator was added, their "blood" is uninfected. If it turns red, the "blood" is infected with HIV. Have students discuss their thoughts about what it would be like to test positive for HIV. Encourage the students to discuss their feelings associated with the activity they have just completed.

** Review and practice precautions, techniques, and safety procedures associated with the handling of corrosive liquids.*

Introduction

You probably have had the flu. Although you suffered from the symptoms of this disease, the illness did not last long. You recovered within several days or weeks. Your recovery coincided with the elimination of the disease-causing agent from your body. As the population of the flu virus declined, the symptoms subsided. Eventually, the virus was either eliminated or reduced to numbers that could not produce disease symptoms.

Suppose your body could not rid itself of infection. How would the course of the disease differ? Actually, there are viruses that the human body cannot eliminate; one is called HIV. This is the story of HIV, how it infects people, and the results of infection. Do you know what the acronyms "HIV" and "AIDS" stand for? What have you heard through the media, or from your friends? Here's a chance to measure what you know. Read the following statements and decide if they are *True* or *False*.

- Most people who are HIV positive do not have AIDS.
- HIV infection can be prevented.
- In most cases, symptoms of AIDS appear many years after the initial HIV infection.
- Even without symptoms, an HIV-infected person can transmit the virus.
- Recent discoveries suggest that treatments for AIDS are possible.

How many of these statements do you think are true? They all are. Are you surprised? Suppose you wanted to know more, what areas of science would you need to study?

A History of AIDS

In early 1981, several young people were diagnosed with a type of pneumonia called *Pneumocystis carinii* pneumonia, or PCP. The disease is caused by the *Pneumocystis carinii* fungus. This one-celled organism is a common inhabitant of our environment. Most of us have inhaled this fungus into our lungs. Yet, its presence does not normally produce pneumonia. Instead, the population of this potentially dangerous microbe is kept in check by our body's defenses. But, for those young people, just breathing the air became dangerous.

The people who were suffering from PCP also experienced symptoms of other diseases. These diseases, like PCP, were caused by microbes that ordinarily were kept in check by the body. Something was wrong with their natural defenses; their bodies could no longer control the populations of potentially deadly microbes.

Doctors did not know what caused the diseases, but the patients all had weakened immune systems; they labeled this illness "Acquired Immune Deficiency Syndrome," or AIDS. AIDS represents a variety of diseases with many symptoms. These diseases are mostly associated with microbes that exploit the body's crumbling defenses. As the illness progresses, more and more of the body's immune system fails.

AIDS doesn't stop with pneumonia. Many microbes that usually are not dangerous begin to establish themselves in the body. A frightening collection of diseases often develops from diverse kinds of microbes. Protozoa, fungi, bacteria, and additional viruses invade the body causing symptoms that can include: weakness; inability to eat; diarrhea; sores on

the mouth, genitals, and skin; seizures; personality changes; and extreme weight loss. Cancers also can develop in the body, causing symptoms such as skin lesions, headaches, and brain damage. Eventually, the cumulative effect of these infections is death.

After much research, scientists identified the virus that caused the immune system to break down in the first place. They called it Human Immunodeficiency Virus (HIV). After a person is infected with HIV, he or she may not start to feel ill for up to 10 years. During those 10 years, however, the HIV-infected person may infect other people with the virus. Nearly all cases (about 19 in 20) of HIV infection will progress to AIDS.

Today, AIDS is a leading cause of death in children and young adults. There have been more than 300,000 AIDS-related deaths in the United States alone. More than 20 million people worldwide may now be carrying the virus that produces AIDS. The World Health Organization estimates that 30 million people around the world will be HIV-infected by the year 2000.

There is some good news. Scientific investigation of the ways that HIV attacks human defenses has generated tremendous new knowledge of the way our immune systems function and the way viruses work. This knowledge helps doctors and scientists find ways to prevent HIV infection and to prolong the lives of people with AIDS.

How to Learn More

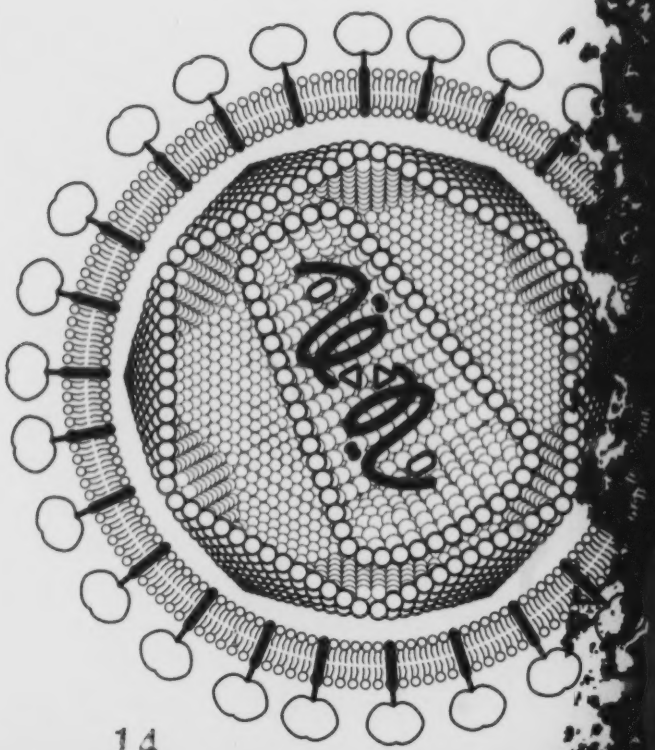
What has been learned about HIV and AIDS? What exactly is HIV? How does it bring about its deadly effects? Is there a way of protecting ourselves from infection? And if we do get infected, what sort of treatment is available?

To help you understand HIV and AIDS, this book is organized into six chapters:

Chapter One	A Healthy Cell: Selected Topics in Cell Biology
Chapter Two	The Virus: A Dangerous Piece of Information
Chapter Three	The Immune System: Defending the Healthy Cell
Chapter Four	Disease Transmission: HIV Infection and AIDS
Chapter Five	Inside the Lab: HIV Diagnostics and Therapeutics
Chapter Six	Outside of the Lab: Communication and Prevention

As you begin your study, you'll find that the chapters begin with general concepts. Once you have a solid foundation, the focus shifts to the specifics of HIV and AIDS. Although you may not know a great deal about this subject right now, you will soon be an expert.

The Science of HIV



TEACHER SUMMARY

CHAPTER ONE

A Healthy Cell

Selected Topics in Cell Biology

Curriculum Connections

- Eukaryotic Cell Structure and Function
- Genes and Chromosomes
- DNA and RNA
- Amino Acids
- Protein Synthesis

Chapter Concepts

Chapter One presents selected topics in cell biology as an overview of processes related to viral infection of eukaryotic cells. The activities are designed to enhance a more complete curriculum on cell biology. The major concept for students to understand is that a cell manufactures its own essential proteins. The blueprints for proteins are in the cell's DNA. DNA is transcribed to become mRNA, translated into protein by tRNA and ribosomes. When viruses (including HIV) infect a target cell, they reprogram the cell's protein synthesis to make viral proteins. When a cell is infected with a virus, sooner or later it deteriorates (it is no longer a healthy cell).

National Science Education Standards

Content Standards 9–12

Content Standard B: Structure and Properties of Matter; Chemical Reactions

Content Standard C: The Cell; Molecular Basis of Heredity; The Interdependence of Organisms; Matter, Energy, and Organization in Living Systems

Content Standard G: History and Nature of Science; Historical Perspectives (Molecular Biology)

A Healthy Cell

Selected Topics in
Cell Biology

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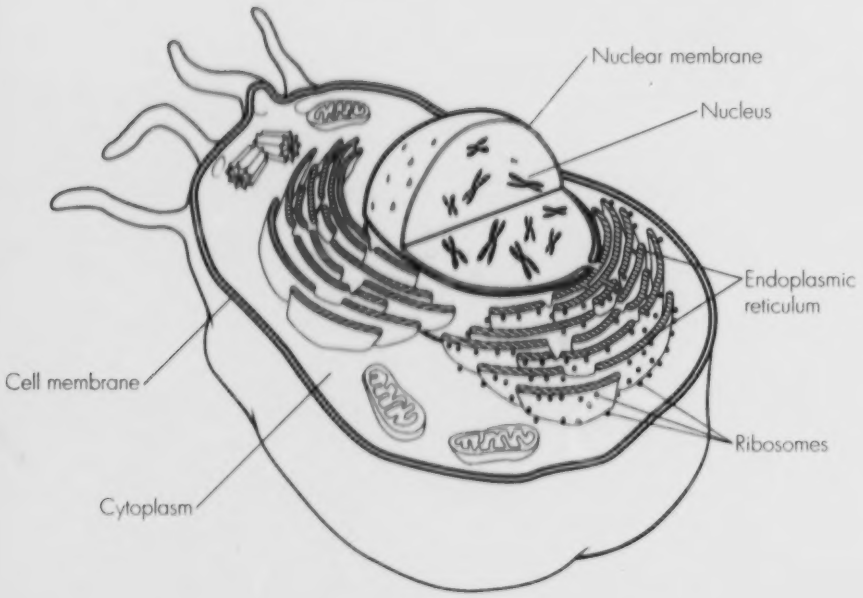
Cells and Viruses

An Overview

Cells are like treasure ships loaded with a rich bounty. The cellular riches are not made of silver or gold. Instead, the cell's wealth resides in its nutrient content and biochemical machinery.



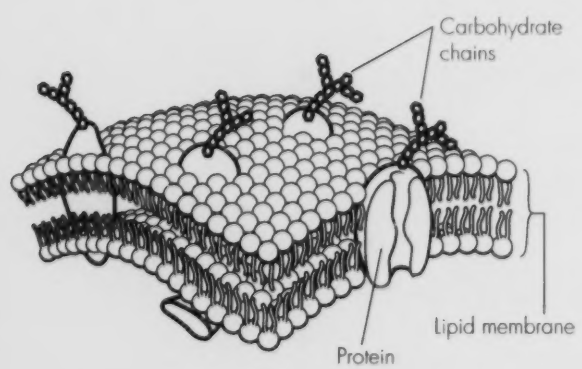
Eukaryotic cell structure

In many-celled organisms, the cells all work together. Through interaction, the cells maintain the health of both the individual cells and the entire organism. A healthy organism has cellular wealth that is appealing to outside attackers. During an assault, healthy cells may be injured or killed. If enough cells are destroyed, the health of the entire organism may be jeopardized.

Microscopic pirates use several tactics to steal a cell's fortune. The largest attackers use brute force to surround and engulf the smaller cell. Once engulfed, the cell is broken down by powerful chemicals.

Cells can be defeated from the inside. Small attackers called parasites infect host cells and plunder the nutrient store. The smallest attackers, however, are not after stored riches. Instead, they target the cell's production factories. These parasites are called **viruses**.

When a virus enters a cell, it hijacks the cell machinery. Some viruses stop the cell from producing materials essential for its own growth and repair. Instead, the cell becomes a virus production factory.



Cell membrane

There are several cell parts that are key to the success of a virus takeover. If these cell parts are deactivated, destroyed, or in some way cloaked, the virus attack fails. If a virus cannot infect a cell, it cannot replicate. Without replication, the infection cycle ends, and the cell is healthy again.

The Cell Membrane

In order to infect a cell, the virus, or parts of the virus, must pass through the cell's outer boundary. This enclosure is called the **cell membrane** or **plasma membrane**. The cell membrane controls what enters and leaves the

cell. The fabric of this boundary is formed by two layers sandwiched together. These layers are made of **lipid**, or fat, a type of material that doesn't dissolve in water.

The surface of the plasma membrane is not smooth. Like chocolate chips in a cookie, **proteins** are embedded into the lipid membrane. Some of these **integral proteins** form channels. Materials cross the lipid membrane through these channels. Other integral proteins can activate hidden passageways. When a substance binds to these proteins, a section of the membrane forms a passageway through which the foreign material enters the cell.

Carbohydrate chains also project outward from the membrane. Both the carbohydrates and proteins can be read by other cells as identity markers. These surface markers help a cell distinguish one cell from another.

COURTESY OF NIAID, NIH

HIV budding out of an infected cell

VIRUSES

If you looked for the parts of a cell in a virus, you'd be disappointed. Not only are viruses small, but they are meager in content. Most viruses contain only two types of substances: proteins and nucleic acids. Viruses lack cell structures such as nuclei, ribosomes, and endoplasmic reticulum. Without this cell machinery, viruses cannot manufacture the materials from which they are formed.

So, to make copies of themselves, viruses must use the machinery of the cells they infect. Within the host, the virus reprograms the genetic code of living cells. New commands instruct the cell's ribosomes to build a new type of material needed to make more viruses—viral protein.

The Nucleus

A virus that passes through the cell membrane enters the cell's **cytoplasm** (the contents between the plasma membrane and the nucleus). Scattered within the cytoplasm are structures called **organelles**. Organelles have varied functions. The most noticeable organelle is *the big one*—the **nucleus**.

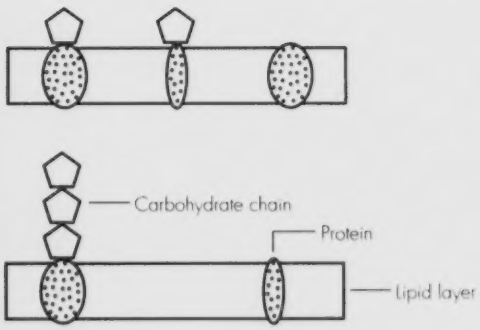
The nucleus stores the "blueprints" for the entire organism. When cell parts are needed, the blueprints are copied. The blueprint copies are dispatched from the relative safety of the nucleus into the surrounding cytoplasm, headed for the ribosomes.

Ribosomes

Much of the cytoplasm contains a canal system called the **endoplasmic reticulum**, or ER. Some parts of the ER appear rough. The roughness is due to the presence of tiny granular structures called **ribosomes.**

Ribosomes are protein factories that manufacture most of the materials (proteins) needed by the living cell. The arrival of the cell's blueprint copies from the nucleus signal the ribosome to begin construction of proteins according to the blueprint.

Questions



Cell membranes

1. Examine the two diagrams of a cell membrane at left. How do these membranes differ? How are they the same?
2. Explain how one cell can be distinguished from another.
3. Suppose a cell's ribosomes were inoperative. How would this affect the cell?
4. Why aren't the original blueprints for manufacturing protein sent out of the nucleus?

Think About It

Why must each cell of a multicellular organism meet both its own needs and the needs of the entire organism?

Cells and Viruses

An Overview

Objective

Students will examine a diagram of the eukaryotic cell and answer questions about the structures and functions of the cell that are necessary for viral infection.

Teacher Notes

The main point for students to understand is that a healthy cell manufactures its own proteins. A virus-infected cell is taken over and reprogrammed to produce viral proteins (but not always exclusively viral proteins). A cell that does not make its own proteins is not meeting its own needs or the needs of the entire organism, putting both in jeopardy.

Discuss the similarities and differences among cells. For the purposes of this book, limit the discussion to eukaryotic/animal cells, particularly human cells. Have students identify the structure and function of cell organelles. Direct student attention to organelles and cell parts that are critical to virus infection and replication: the cell membrane, the nucleus, and the ribosomes. Discuss how protein and carbohydrate markers signal a cell's identity to other cells.

Challenge students to construct a three-dimensional model of the cell membrane. The model should illustrate the lipid bilayer, integral proteins, and carbohydrate projections.

Assessment

Have students compose an essay about a voyage through a cell. If time allows, discuss the novel by Issac Asimov, *Fantastic Voyage*, in which a submarine and its scientist crew are miniaturized and injected into a human body to remove a blood clot to save a man's life. In their free time, students might enjoy watching the movie, *Fantastic Voyage*, or the more recent movie, *Inner Space*. They could critique the movie(s) for how realistically principles of cell biology are portrayed.

Answers to Student Questions

1. Both contain a lipid bilayer, embedded proteins and carbohydrate chains. They differ in the identity and placement of proteins and carbohydrates.
2. Each cell possesses a unique assortment of membrane markers.
3. The cell could not produce proteins for cell structure and function. Eventually, the cell would die.
4. The original blueprints remain within the relative safety of the nucleus so that they are not damaged.

Answer to Think About It

The cells of an organism help it stay alive. If enough cells die, the whole organism dies. This question foreshadows the discussion of HIV infection in later chapters. HIV eventually kills human immune cells. When enough immune cells die, the person dies.

INTEGRAL PROTEINS IN THE CELL MEMBRANE

The cell membrane contains large embedded molecules called integral proteins. Membrane proteins perform a variety of functions. Some integral proteins provide a channel through the membrane core. These "transport proteins" produce the selective permeability of the plasma membrane. Other integral proteins have a role in maintaining cell shape and catalyzing reactions. Integral proteins that are receptor sites bind to external molecules of neighboring cells. This reaction may initiate the entrance of molecules into the cell. An example of a receptor protein is CD4. CD4 is one of the proteins to which HIV binds to gain entrance to Helper T lymphocytes in the human body. (CD4 alone does not make a cell infectible by HIV; other co-factors are needed.) Thus, a normally occurring receptor protein allows HIV to infect its host cells.

Vocabulary

cell membrane (also called plasma membrane) - exterior lipid membrane that separates a cell from its surroundings

carbohydrates - monomers and polymers composed of carbon, oxygen, and hydrogen atoms

cytoplasm - the material surrounding the nucleus and contained by the cell membrane; area where most organelles are located

endoplasmic reticulum (ER) - tubular channels that are associated with the intra-cellular manufacture and transfer of materials

integral proteins - proteins embedded into the cell membrane that help cells recognize each other and also transport materials in and out of the cell

lipids - molecules such as fats, oils, and waxes

nucleus - membrane-bound control center of cell; contains DNA

organelles - internal membrane-bound structures within a cell

protein - complex organic molecule composed of many amino acids

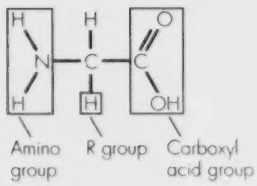
ribosomes - molecular complexes associated with protein synthesis

virus - non-living infectious particle containing only proteins and nucleic acids

A Cell Product

Protein

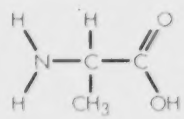
Suppose you removed the water from a living cell. What types of molecules would remain? You'd uncover complex molecules called **macromolecules**. Macromolecules include starches, lipids, nucleic acids, and proteins. The cell makes most of these materials from the materials it obtains from the world outside the cell membrane.



Glycine

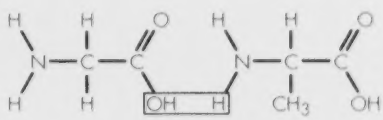
Proteins are the most common macromolecules, making up more than half of a cell's dry weight. A cell cannot function without making new proteins. Proteins provide a cell's structure, transport chemicals, and help it fight infection.

The structure of a protein is a long chain of repetitive building blocks called **amino acids**. Like roller coaster cars, a protein molecule is formed by amino acids that are hooked together. The chains that make up different kinds of proteins can consist of 50 to more than 50,000 individual amino acids. Additionally, there are 20 different types of amino acids. The length (how many amino acids) and composition (what kinds of amino acids) of each chain are critical. If just one amino acid is in the wrong place or is the wrong type, the entire chain may be useless.



Alanine

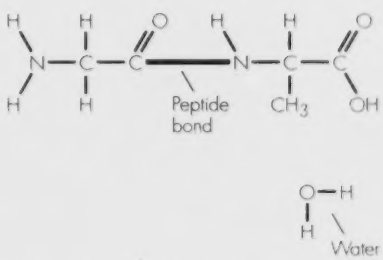
All amino acids contain an **amino group** and a **carboxyl group**. An attached side chain called the **R group** provides the difference between amino acids. **Glycine** is the simplest amino acid; its R group consists of a single hydrogen atom. Another amino acid, **alanine**, has an R group of one carbon and three hydrogen atoms.



Amino acids aligned to be joined

Amino acids that are to be joined are arranged side-by-side. The amino group of one aligns with the carboxyl group of the other. The OH group from the carboxyl group and the H atom from the amino group react to form a molecule of H_2O (water).

As the atoms that compose water are removed, a new bond forms between the adjoining amino acids. This new bond is called a **peptide bond**.

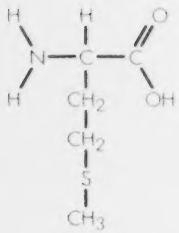


Peptide bond forms between joined amino acids

Questions

1. An _____ and a _____ are found on opposite sides of an amino acid.

2. A _____ is the chemical link between neighboring amino acids.



Methionine

3. This diagram represents the amino acid methionine. Circle and label its amino group, carboxyl group, and R group.

Think About It

What would happen to a cell if a virus reprogrammed the cell's protein synthesis?

A Cell Product

Protein

Objective

Students will read about and answer questions about basic protein structure and why proteins are essential to a healthy cell.

Teacher Notes

Students should know that proteins carry out essential cellular roles such as transport, structure, and immune functions. The main point is that a cell must produce its own proteins to live, and to sustain the needs of the entire organism. For example, some viruses, such as herpes viruses, shut down host cell protein synthesis and force the cell to exclusively produce viral proteins. In contrast, HIV shares the protein machinery with the host cell, permitting the cell to carry on normal functions while also producing viral particles. HIV-infected cells eventually die, but it is not known precisely why.

Explain that the word protein comes from *protos*, the Greek word meaning "of prime importance." Review the presence and role of various body proteins, including hemoglobin, insulin, keratin, actin, and myosin.

A pop-bead necklace can be used to demonstrate the relationship between individual amino acids (monomers) and the protein chains (polymers) they form. Individually, the beads represent amino acids. The joining of the beads depicts the formation of a polypeptide chain.

For advanced students, you may wish to explain that proteins have four levels of structure:

a. primary structure - the linear sequence of amino acids
b. secondary structure - the folding of polypeptide chains due mostly to hydrogen bonding (see box)
c. tertiary structure - contortion of the chains into complex three-dimensional shapes
d. quaternary structure - large proteins consisting of several protein strands in tertiary structure

Most biology textbooks contain good explanations and figures of protein structure and function.

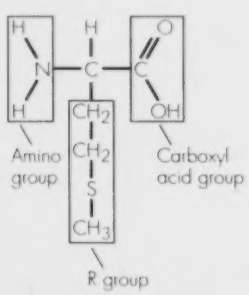
HYDROGEN BONDING

Atoms and molecules can interact in different ways, and the strength of these interactions can vary considerably. Hydrogen bonding is a relatively weak type of attraction that results from the unequal sharing of electrons. When hydrogen forms a covalent bond with oxygen, the bonding electrons are not shared equally. Instead, they spend more time nearer the oxygen nucleus. This uneven distribution of charge creates a dipole. The hydrogen takes on a slight positive charge; the oxygen acquires a negative charge. Although slight, interactions between the positive and negative charges create three-dimensional structural effects in proteins.

These structural effects can be observed in both the secondary and tertiary structures of proteins. In the secondary structure, hydrogen bonding influences the arrangement between two distinct amino acid chains. In tertiary structure, hydrogen bonding along with hydrophobic interaction and disulfide bridges produce a complex, contorted shape.

Answers to Student Questions

1. Amino group, carboxyl group
2. Peptide bonds
3. See chemical structure at right.



Answer to Think About It

Viruses generally cannot use the protein manufactured according to host cell blueprints. Viruses must force the cell to manufacure viral proteins to replicate more viruses. If a cell is making proteins exclusively for the virus, it usually cannot replenish its own protein needs and eventually deteriorates.

Vocabulary

amino group - an NH_2 functional group on an amino acid

amino acid - building block of protein that contains both an amino group and a carboxyl group

carboxyl group - a COOH functional group on an amino acid

macromolecule - large molecule built from small chemical structures

peptide bond - chemical link between adjoining amino acids

R group - attached side chain on an amino acid which distinguishes an amino acid from others

The Blueprints of the Cell

Nucleic Acids

Which of the following two sentences makes sense?

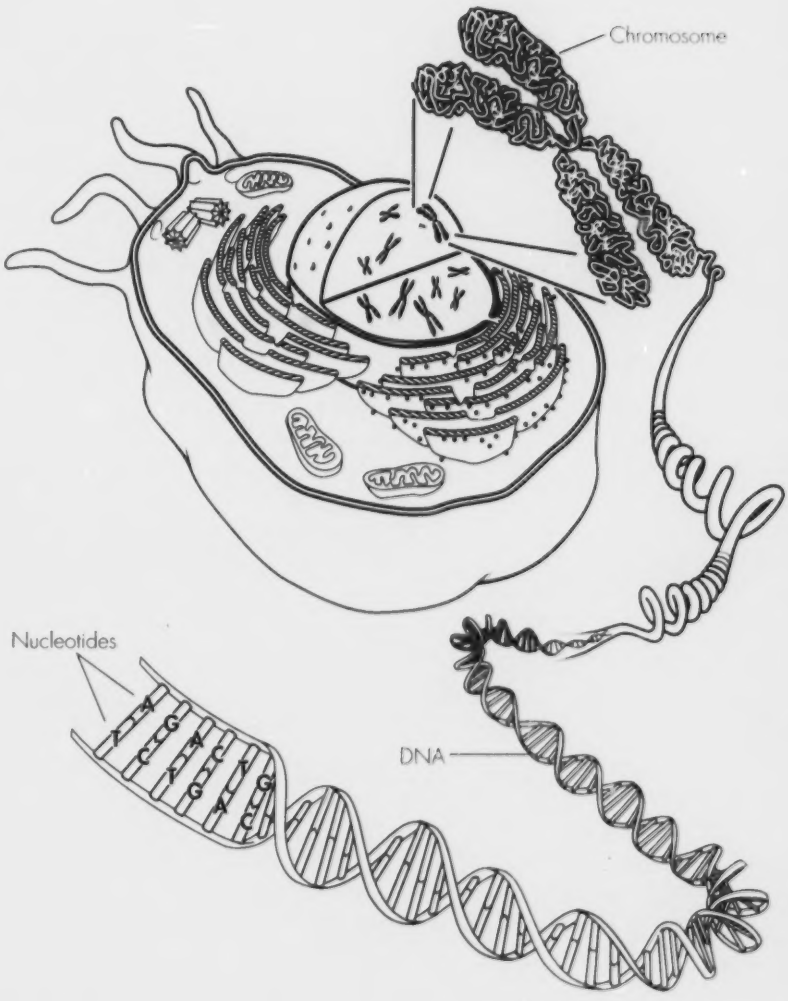
Words are formed by letters placed in proper order.

Dropy poodsin mae fetr tesarcber rolwdperr redel.

Obviously, the first sentence makes sense. Although the letters in both sentences are exactly the same, their order is different. This order is essential for us to understand the meaning of the sentence. Without a recognizable pattern, the letters, words, and sentence are meaningless.

Proteins, like the sentences above, must be formed by a specific sequence of amino acids. There can be no mistakes. If a single amino acid is misplaced or missing, the entire protein may be useless. Your body contains tens of thousands of different proteins. Each protein has its own sequence of amino acids. Each sequence has its own blueprint.

When a cell requires proteins, it must access specific blueprints on a **chromosome**. Each blueprint for a specific protein occupies a site on a chromosome called a **gene**. When a blueprint is needed, its information is copied onto a messenger molecule. This molecule leaves the nucleus and transports the blueprint copy to the ribosomes in the cytoplasm.



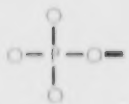
When a virus invades a cell, it replaces the cell's blueprints with its own construction plans. When the viral blueprints arrive at ribosomes, they are treated as if they are the cell's own code. The reprogrammed ribosomes follow the code's instructions and build viral proteins.

Viruses and cells are two very different things. Yet, they share a common chemical language recorded in macromolecules called nucleic acids. There are two types of nucleic acids, **DNA** and **RNA**.

Deoxyribonucleic Acid (DNA)

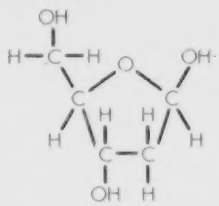
DNA is found mostly in the nucleus; it is the code for every protein manufactured by the cell. DNA is a replicating molecule. In other words, if supplied with the right materials, it can make copies of itself.

Like protein, DNA consists of a chain of subunits called **nucleotides.** There are four different DNA nucleotides; each one contains three chemical parts: a phosphate group, a sugar, and a nitrogenous base (nitrogen-containing).



Phosphate group

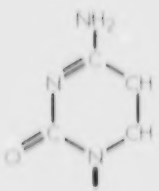
The phosphate group is composed of three oxygen atoms attached to a central atom of phosphorus.



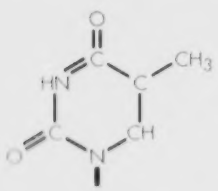
Deoxyribose sugar

The sugar of DNA is deoxyribose sugar. Like other ribose sugars, deoxyribose contains five carbon atoms.

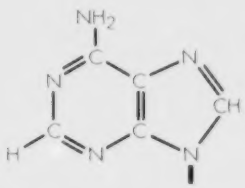
The four different nitrogenous bases found in DNA nucleotides are:



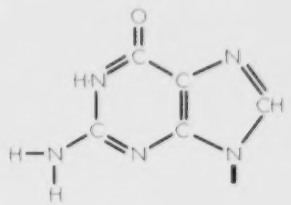
Cytosine



Thymine

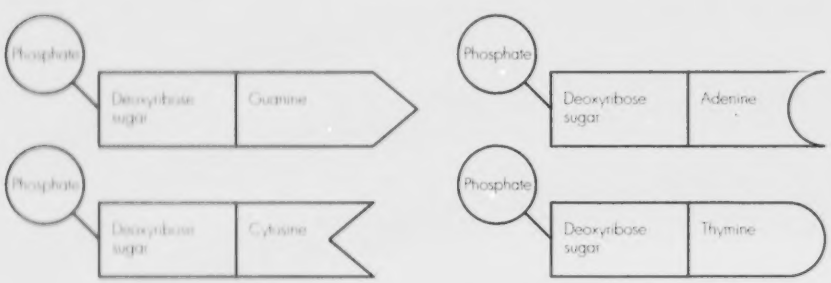


Adenine



Guanine

This type of structural diagram can get complex. To make things simpler, a type of shorthand can represent the nucleotides:



Ribonucleic Acid (RNA)

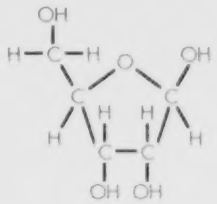
RNA is the second type of nucleic acid. Unlike DNA, RNA is located in the cell's nucleus, but also in the cytoplasm and in the ribosomes. RNA is an active player in the synthesis of protein. There are three types of RNA:

messenger RNA (mRNA) - copies of DNA become mRNA which transports the code to the ribosomes.

transfer RNA (tRNA) - tRNA ferries amino acids to the ribosomes.

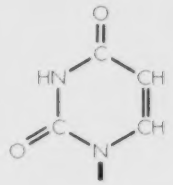
ribosomal RNA (rRNA) - rRNA is a structural material that makes up the ribosomes.

Like DNA, RNA is composed of nucleotide building blocks. These nucleotides are slightly different than their DNA counterparts. Although the phosphate group is identical, the sugar is ribose sugar, not deoxyribose sugar.



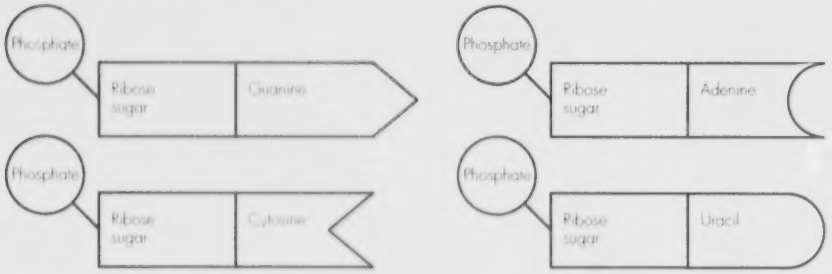
Ribose Sugar

There are four RNA nitrogenous bases. Three bases are the same as DNA bases: adenine, guanine, and cytosine. Thymine is not an RNA base. Thymine is replaced by a base of similar structure, uracil.



Uracil

The four RNA nucleotides may be represented as:



Questions

1. What is a nucleotide?
2. What is a gene?
3. Compare and contrast DNA with RNA.
4. Describe the three types of RNA.

Look carefully at the chemical structures on pages 14 and 15.

5. Which bases are composed of two ring-like structures?
6. What is the structural difference between thymine and uracil?
7. What is the structural difference between ribose sugar and deoxyribose sugar?

The Blueprints of the Cell

Nucleic Acids

Objective

Students are introduced to and answer questions on the structure and function of DNA and RNA.

Teacher Notes

Display a set of architectural blueprints. They may be available from a drafting teacher or a real estate agent. Have students discuss how these blueprints are used to build a structure. Then challenge students to make an analogy between construction blueprints and the code for an amino acid sequence embedded in the DNA molecule.

Explain that the cellular content of DNA varies from organism to organism. There are, however, some trends that reflect the complexity of the organism. The table below lists the approximate number of nucleotide pairs found in viruses and in the individual cells of humans. A bar chart can also illustrate the huge difference in genetic material between humans and viruses.

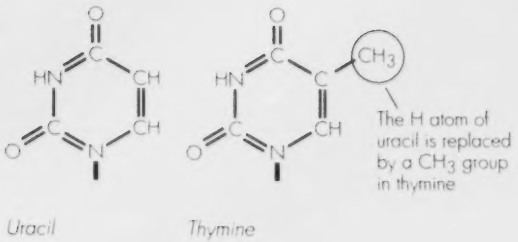
Organism	Nucleotide pairs	
virus	10^4	10,000*
humans	$4x10^9$	4,000,000,000

**The number of nucleotide pairs in animal viruses can vary from approximately 8,000 to 190,000.*

Answers to Student Questions

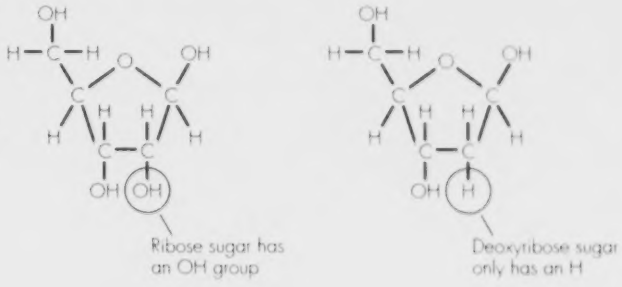
1. A building block of nucleic acid
2. A chromosome site that contains the blueprint for a specific protein
3. DNA is a replicating molecule that stores the protein blueprints. RNA has several forms that play a role in the manufacture of protein. Both molecules contain a code that can be translated by the ribosome.
4. mRNA carries a copy of the DNA code. tRNA ferries amino acids to the ribosomes. rRNA is a structural component of ribosomes.
5. Guanine and adenine

6.



Uracil *Thymine*

7.



Vocabulary

adenine - nitrogenous base component of the adenine nucleotide; found in both DNA and RNA; complement to thymine

chromosome - a DNA-containing molecule of the cell's nucleus by which hereditary information is transmitted

cytosine - nitrogenous base component of the cytosine nucleotide; found in both DNA and RNA; complement to guanine

DNA (deoxyribonucleic acid) - replicating molecule, double-stranded nucleic acid that contains deoxyribose sugar

gene - site on a chromosome that codes for a specific protein

guanine - nitrogenous base component of the guanine nucleotide; found in both DNA and RNA; complement to cytosine

messenger RNA (mRNA) - a copy of DNA; transports the copy to the ribosomes

nucleotides - building blocks of nucleic acids

RNA (ribonucleic acid) - single-stranded nucleic acid that contains ribose sugar

ribosomal RNA (rRNA) - structural molecule from which the ribosomes are constructed

thymine - nitrogenous base component of the thymine nucleotide; found only in DNA; complement to adenine

transfer RNA (tRNA) - ferries amino acids to the ribosomes

uracil - nitrogenous base component of the uracil nucleotide; found only in RNA; complement to adenine

Building DNA with Nucleotides

You probably grew up with scale models such as toy cars, miniature planes, dolls, and doll houses. They have the appearance of an actual object, but are much smaller in size. Scientists also use scale models. Many of their models, however, aren't scaled *down* versions of real things. These laboratory representations are *scaled-up* renderings.

Molecules are wonderful subjects for model building. Since they are too small to be observed directly, scientists infer their appearance from laboratory analysis. This information is used to build a scale model that represents some aspect of the molecule. By observing a scale model, scientists can obtain a better understanding of objects too small to be seen. In this activity, you'll have the opportunity to learn about DNA by constructing a scale model of this molecule.

Part A: Nucleotide Models

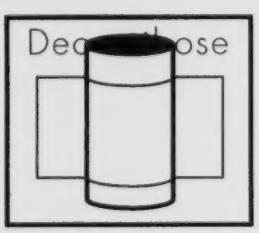
All DNA and RNA nucleotides are composed of a nitrogenous base, a five-carbon sugar, and a phosphate group. Although similar in structure, these nucleotides differ in the type of bases and sugars that compose them.

In this activity, you will construct models of nucleotides. In following activities, you will use these models as building blocks to assemble representations of DNA and RNA. You will also use them to illustrate steps of DNA replication and protein synthesis.

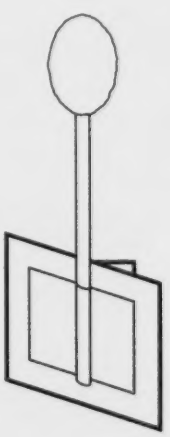
Materials

cotton swabs
nucleotide component sheet (copied or pasted onto heavy stock paper), pg. 20
straws
scissors
tape

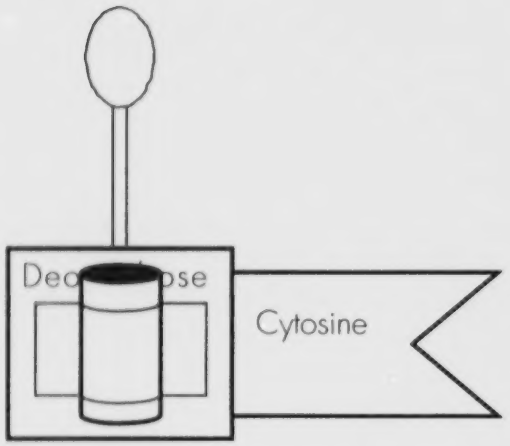
DNA Nucleotides



1. Work with a partner. On the nucleotide component sheet, identify the sugars and nitrogenous bases. Cut out one paper square that represents deoxyribose sugar.
2. Cut out several small sections of straw about 1 centimeter in length.
3. Use tape to attach one section of straw to the square, as shown at left.
4. Remove and discard one of the tufts from a cotton swab. Use tape to secure the stripped end of the swab to the sugar, as shown at right. The tuft represents the phosphate group. The swab should be taped to the other side of the square.



5. Cut out a representation of a cytosine base. Use tape to attach the base to the sugar as shown here.
6. Complete the three additional DNA nucleotides—adenine, thymine, and guanine.



RNA Nucleotides

1. Cut out one paper square that represents ribose sugar.
2. Cut out several small sections of straw about 1 centimeter in length.
3. Repeat steps 2–5 to construct a model of the RNA cytosine nucleotide.
4. Complete the three additional RNA nucleotides—adenine, uracil, and guanine.

Nucleotide Model Sets

Construct three complete sets of DNA nucleotides and two complete sets of RNA nucleotides, plus an additional uracil nucleotide. Store all of your nucleotides in a safe place.

Questions

Use the DNA nucleotide models to answer the following questions.

1. How are the nucleotides similar?

2. How are the nucleotides different?

3. How would you sort the four DNA nucleotides into two groups based upon size?

Use the RNA nucleotide models to answer the following questions.

4. How are the RNA and DNA nucleotides similar?

5. How are the RNA and DNA nucleotides different?

6. Which RNA nucleotide replaces the DNA thymine nucleotide?

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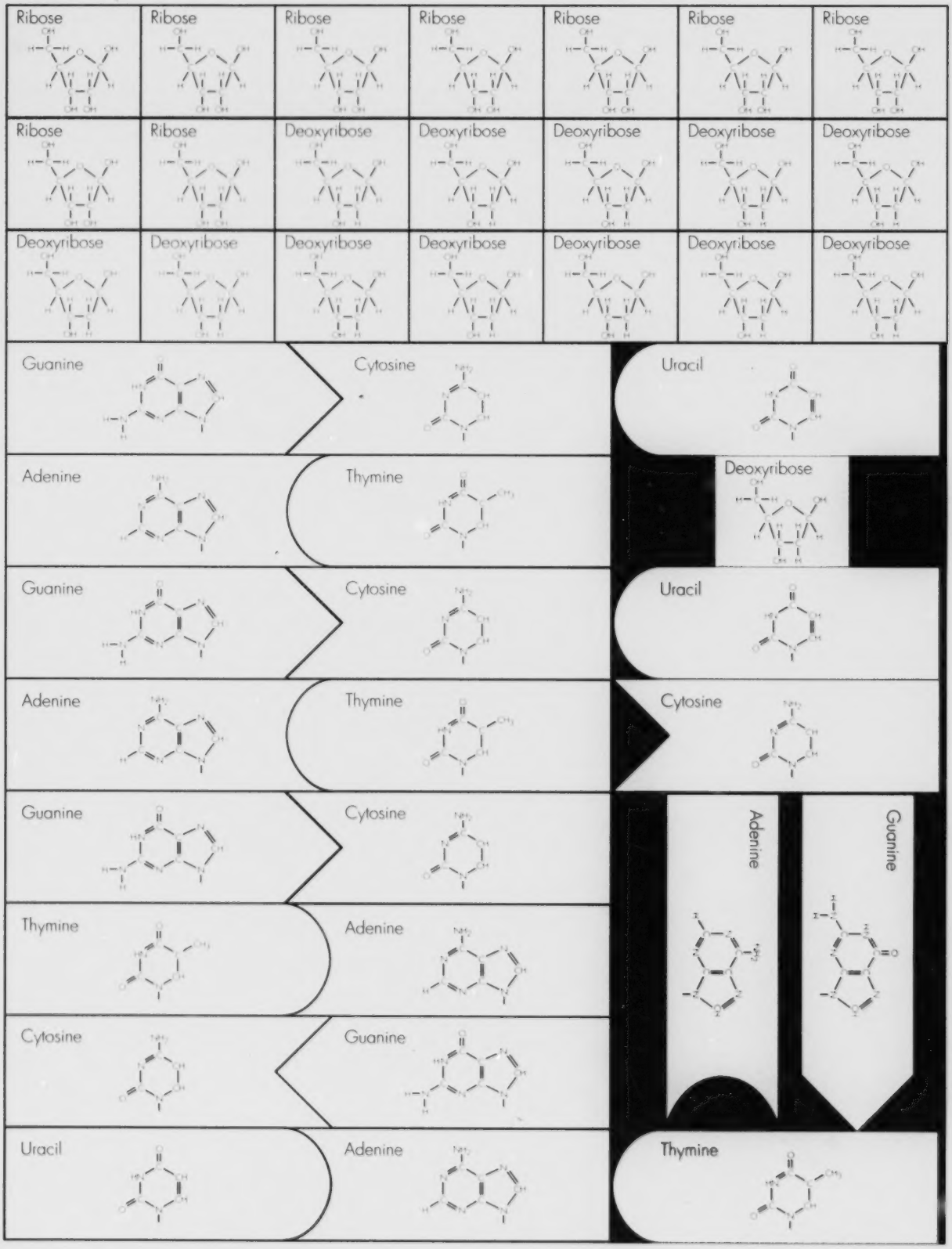
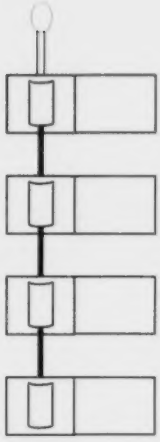
Nucleotide Components



Part B: A Model of DNA

Nucleotide Sequence



1. From your collection of nucleotide models, remove four different DNA nucleotides.
2. Insert the cotton tuft of one nucleotide into the straw collar of an adjoining nucleotide.
3. Continue connecting the nucleotides until all four are joined. Sketch the sequence of nucleotides, with the names of the bases, in the box at the right.

Sketch sequence of DNA nucleotides

Complementary Bases

By now, you may have observed that some outer edges of the bases have counterpart shapes. The projection of one base fits the hollow of another. Although these are only paper models, they reflect a similar coupling at the molecular level. This type of "fit" produces complementary base pairs.

Examine the exposed edge of each base of your DNA sequence. Then write the name of the complementary base next to each base below.

adenine - _____

cytosine - _____

thymine - _____

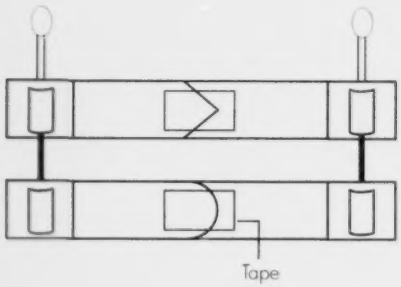
guanine - _____

Use your collection of DNA nucleotides to build a complementary strand of DNA. Sketch the complementary nucleotide strand in the box at the right.

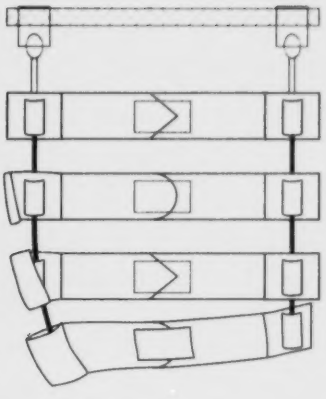
Sketch complementary strand of DNA nucleotides

Hydrogen bonds

The bonds that form between these complementary base pairs are **hydrogen bonds.** Hydrogen bonds are relatively weak bonds. However, since there may be millions of base pairs in a strand of DNA, the collective force of the hydrogen bonds is strong enough to keep complementary strands together.



To simulate hydrogen bonding, use small pieces of tape to join complementary base surfaces.



Double Helix

The double-stranded DNA molecule is not flat. It takes on the form of a shape called a **double helix** resembling a spiral staircase. Using your complementary strands, here is how to put a spiral staircase "twist" into your model.

1. Use tape to secure the upper cotton tuft from each base sequence to an overhanging support.
2. Place a slight twist in the ladder. Adjust its height so that the bottom of the ladder touches the desktop. Use tape to secure the bottom of the twisted model to the surface of the desk.

DNA Replication

Now that you know what DNA looks like, use your model to illustrate how this molecule replicates.

WHAT REAL DNA DOES	MODEL DNA
Uncoiling The first step in DNA replication is uncoiling.	***Uncoiling*** To represent this step, undo the twist that you placed in your model.
Separating Strands Next, the strands are "unzipped" by special enzymes. Additional proteins wedge in between the "unzipped" strands. This chemical "wedge" forms a physical block that prevents the strands from rejoining.	***Separating Strands*** Carefully undo the tape that joins complementary bases. The tape represents the hydrogen bonds that keep the strands together.
Adding New Nucleotides After the strands have been "primed," enzymes, called **DNA polymerases**, go to work. These enzymes catalyze the addition of nucleotides onto the exposed bases. Since the new nucleotides can only pair with their complementary base, the order of the sequence is maintained.	***Adding New Nucleotides*** From your collection of nucleotides, add a sequence of four DNA nucleotides to only one of the exposed strands. Although in reality new nucleotides will attach to both strands, we'll just concentrate on one. Tape up the new strand of DNA. As you can see, it is formed from both an old strand, and a newly synthesized complementary strand.
Recoil Finally, the pairs of complementary strands coil into two copies of the original double helix.	***Recoil*** Place a slight twist in its form and the new double helix is complete.

Building DNA with Nucleotides

Objective

Students will construct nucleotide models and a model of DNA to extend their understanding of nucleic acid composition and structure. Later, students will use the models to illustrate DNA replication and transcription.

Teacher Notes

Part A: Nucleotide Models

Have students discuss the similarities and differences among the DNA and RNA nucleotides. These models will be used in Part B and activities in Chapter Five to illustrate biochemical structures and events.

Part B: A Model of DNA

The extra deoxyribose sugar and thymine base is for the AZT activity in Chapter Five. When students connect nucleotides with tape, use masking tape or white artist tape so that the DNA strands can "unzip." Review the concept of a nucleotide sequence. Have students analyze a sequence in terms of a code that it may contain. If appropriate, challenge the class to suggest a model for code duplication.

Answers to Student Questions

DNA Nucleotides

1. All nucleotides are composed of a phosphate group, deoxyribose sugar, and a nitrogenous base.
2. Each of the four nucleotides contains a different base.
3. Adenine and guanine; cytosine and thymine

RNA Nucleotides

4. Both types of nucleotides contain a phosphate group, a sugar, and a nitrogenous base.
5. RNA contains ribose sugar. DNA contains deoxyribose sugar.
6. Uracil

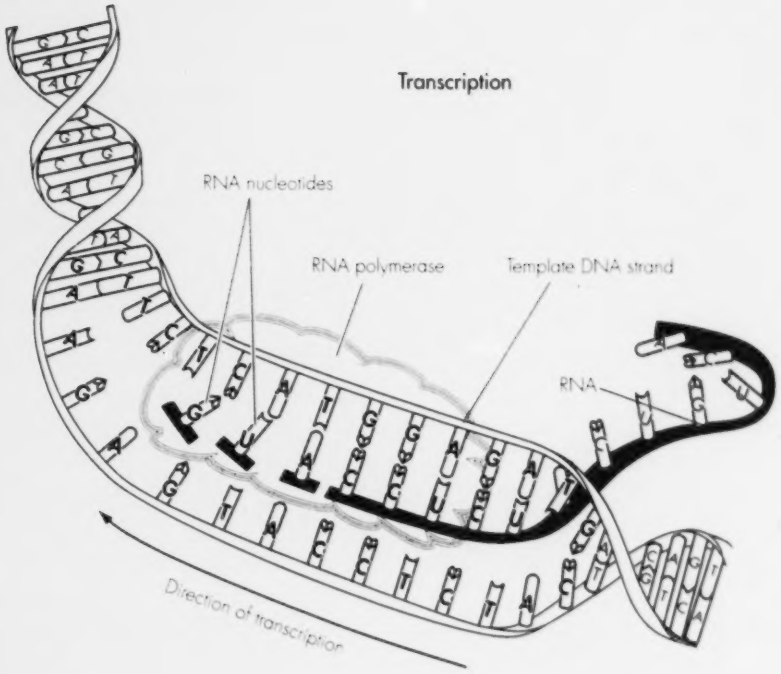
Vocabulary

DNA polymerases - group of enzymes that catalyze the addition of nucleotides during the synthesis of DNA

double helix - a twisted, ladder-like form

hydrogen bond - a relatively weak attraction between a hydrogen atom (positive charge) and an atom with a negative charge, like oxygen

Copying the Blueprints



Blueprints for a building are valuable, so copies are made and the originals are kept in a safe. Similarly, original DNA is kept inside the nucleus. When protein needs to be synthesized, these blueprints are used. Although the DNA information travels into the cytoplasm, the original DNA molecule never leaves the safety of the nucleus.

Within the nucleus, an enzyme called **RNA polymerase** makes a copy of the DNA code. This copying process is called **transcription**, which makes **messenger RNA** (mRNA). Unlike DNA, the transcribed mRNA leaves the nucleus. Prior to leaving the nucleus, mRNA is modified to remove material not needed for protein synthesis. At the ribosome, the mRNA is used to assemble amino acid sequences, making proteins.

DNA Blueprints

Before we can assemble an mRNA molecule model, we need to build an original DNA blueprint containing six base pairs. Using DNA nucleotide models, assemble a single strand of DNA (as if DNA is unzipped) with the following base sequence: ATTGCG.

Question

1. What is the sequence of its complementary DNA strand?

Assemble the complementary strand of DNA. Align the strands so that complementary bases are adjacent. Do not twist the strands or tape the strands together. Sketch the layout of the two complementary DNA strands in the box to the left.

Sketch complementary DNA strands

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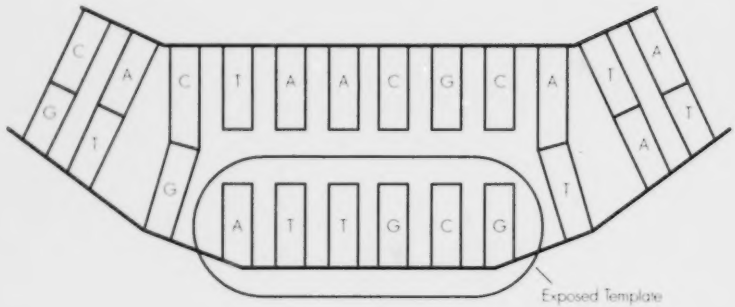
Transcription

During mRNA formation, the double strand of DNA partially separates. This separation occurs where the code will be copied. The exposed base sequence of one strand is used to guide the assembly of mRNA. This sequence of exposed DNA nucleotides is called a **template**.

Separate the two strands of complementary DNA nucleotides. The ATTGCG will be used as the template to guide mRNA construction. The diagram at right illustrates the relationship between this exposed template and the rest of the DNA molecule.

Like their DNA counterparts, the RNA nucleotides align against complementary bases. The base pairing is the same except that RNA has uracil, not thymine.



Question

2. What is the sequence of complementary RNA nucleotides?

Align the RNA bases with their template complements. Once aligned, the RNA nucleotides are linked together by RNA polymerase.

Assemble the complementary strand of RNA. Use the cotton tufts and straws to join the sequence of RNA nucleotides. Sketch the layout of both strands in the box to the right.

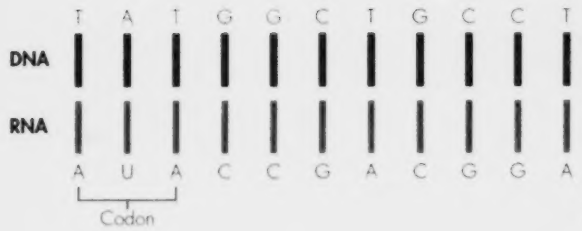
As the strand of mRNA is formed, it peels away from its DNA template. After the code has been copied, the DNA "zips" back up. The fully-formed mRNA is now independent. Its sequence of bases contains genetic code that has been copied from the DNA template. This blueprint copy leaves the nucleus and travels to the ribosomes.

Sketch template DNA and complementary strand of RNA

Copying the Blueprints

Objective

Students model the structure of mRNA to understand how the protein code is transcribed from DNA to mRNA. Students should understand the difference between RNA nucleotides and DNA nucleotides. The main point is that the copy of the DNA (mRNA) moves out of the nucleus and arrives at the ribosomes to be the code for new protein.



Teacher Notes

Students will use their nucleotide models to illustrate the steps of mRNA transcription.

Write the nucleotide sequences at left on the chalkboard. Have students distinguish between the DNA and RNA strand (the RNA strand contains uracil instead of thymine). Challenge students to explain transcription in terms of complementary bases and templates.

Answers to Student Questions

1. TAACGC
2. UAACGC

Vocabulary

mRNA (messenger RNA) - single-stranded nucleic acid copied from double-stranded DNA; transported from the nucleus through the cytoplasm to the ribosomes

RNA polymerase - enzyme that copies DNA into RNA

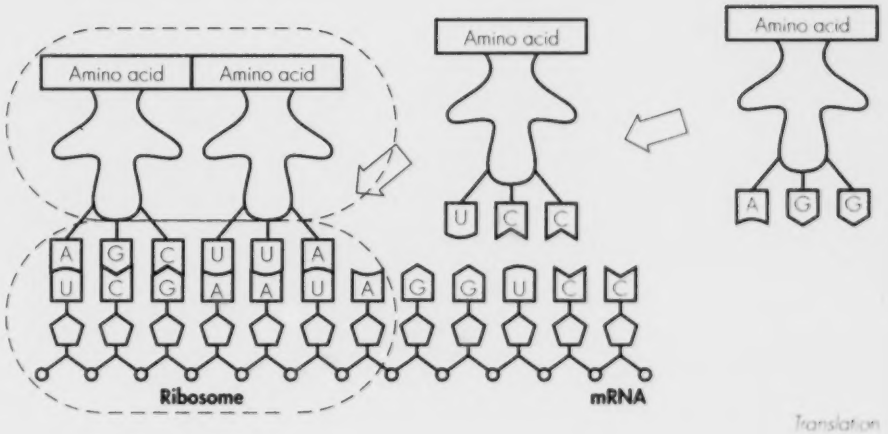
template - exposed sequence of DNA bases on which the complementary nucleic acid strand is synthesized

transcription - the copying of code from DNA to RNA

Delivering Amino Acids to Build Proteins

Part A: Transfer RNA

What good is a building plan without construction materials? By themselves, protein blueprints are useless. To have value, they must be translated into a protein. This **translation** from nucleotide code to protein occurs at the ribosomes.



Translation

To build a protein chain, you need amino acids. Remember that there are 20 different amino acids. Although amino acids are located within the cytoplasm, they must be transported to the ribosomes. The ferrying of amino acids is done by **transfer RNA (tRNA)**. Each tRNA molecule is specific; it can ferry only one kind of amino acid. **The order of the amino acids needed is determined by mRNA code.** According to this mRNA code, a specific tRNA molecule arrives at the ribosome carrying its amino acid. The tRNA places its amino acid at the end of the enlarging protein chain.

The Code

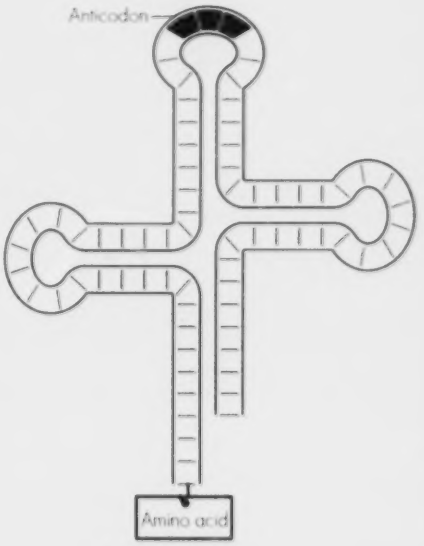
The code used by DNA, mRNA, and tRNA is based upon triplets of nucleotide bases. Three side-by-side bases form a unit called a **codon**. A codon may contain any combination of three bases.

Each codon identifies a specific amino acid or an instruction to stop or start making protein. For example, AGC specifies the amino acid serine. Some amino acids are specified by more than one codon. The codes GUC and GUA both specify valine.

AUG is the only codon that signals "start making protein." It also codes for the amino acid, methionine. Therefore, every amino acid chain begins with methionine. UAA, UAG, or UGA are the three codons that signal "stop." When these codons are reached, the protein synthesis ends and the amino acid chain peels away from the ribosome.

tRNA Structure

tRNA consists of a single strand of RNA nucleotides. This strand is shaped into a cloverleaf design. The base of the cloverleaf has a "molecular hook." The hook attaches to an amino acid. The other end of the tRNA molecule has a special three-base sequence. This sequence is called the **anticodon**. The anticodon is a complement to a codon present on the mRNA strand.



Transfer RNA

40

Questions

1. Examine this sequence of mRNA.
   A-U-G-C-G-A-A-G-G-A-A-A-U-C-A-U-A-G

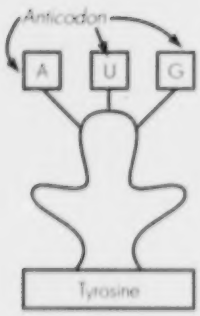
   a. Starting with A-U-G, how many codons are represented by this sequence?

   b. How many amino acids are coded by this sequence?

   c. What does the first triplet signify?

   d. What does the final triplet signify?

   e. Write a complementary RNA nucleotide sequence.



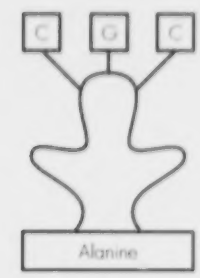
2. The box below illustrates some of the codons and the amino acids that they specify. Use this information to identify the amino acid sequence encoded into the strand of mRNA below the box.

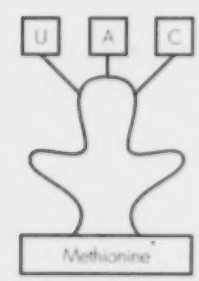
mRNA codons

AAA Lysine	AAU Asparagine	AGC Serine	CGA Arginine
GAU Aspartic acid	GUA Valine	GUC Valine	UUA Leucine

A-U-G-G-U-C-U-U-A-A-A-U-A-A-A-G-U-A-C-G-A-A-G-C-U-A-G

mRNA strand





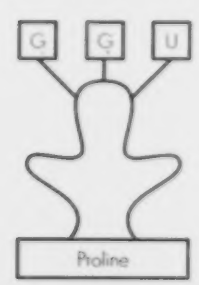
3. Examine the representations of the tRNA molecules at left and answer the questions below.

   a. What codon specifies proline?

   b. What is the anticodon carried by alanine tRNA?

   c. What codon specifies tyrosine?

   d. The codon AUG specifies two things. What are they?



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Part B: Protein Synthesis

DNA blueprints have been copied into single strand mRNA. The mRNA is at the ribosomes ready to begin the production of protein. The process begins with the fit between the mRNA codon and tRNA anticodon. As the tRNA molecules attach to the mRNA strand, amino acids are aligned in their correct sequence. A set of enzymes join the side-by-side amino acids into a lengthening protein chain.

As soon as one amino acid is added to the chain, the next codon binds to its complementary anticodon. The tRNA positions its amino acid cargo. The joining of amino acids continues until the "stop" codon is reached. This signal halts translation and releases the newly formed protein.

Questions

Examine the mRNA molecule and the eight molecules of tRNA represented on page 30 and answer the following questions.

1. Determine the DNA nucleotide sequence from which this mRNA strand was formed.
2. How many codons are present on this example mRNA molecule?
3. What is unique about the first and last codon of an mRNA strand?
4. How many anticodons does each tRNA molecule have?
5. How many different kinds of amino acids can each tRNA transport?
6. What is one anticodon for valine?
7. Suppose an mRNA codon had the sequence AAA. What anticodon would complement this codon? What amino acid would be specified by this code?
8. Number the statements below in proper order.

___ Amino acids are brought to the mRNA/ribosome complex by tRNA.
___ The code for making blueprints is stored on DNA.
___ The genetic code is translated.
___ The DNA code is copied onto a single strand of mRNA by RNA polymerase.
___ The completed polypeptide chain separates from the ribosome.
___ The DNA double helix "zips" closed.
___ mRNA forms a complex with a ribosome.
___ tRNA attaches to an amino acid.
___ Peptide bonds form between adjoining amino acids.
___ The DNA double helix "unzips."
___ mRNA leaves the nucleus and enters the cytoplasm.

RIBOSOMAL RNA

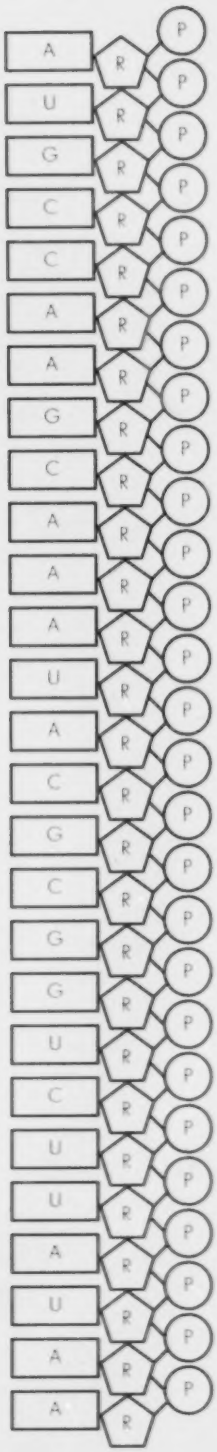
A third form of RNA plays a structural role in the manufacture of proteins. Ribosomal RNA (rRNA) accounts for more than half the weight of each ribosome. rRNA bonds with an assortment of proteins to form the two sub-units of the ribosome. Sites on the ribosome lock onto mRNA, tRNA carrying the polypeptide chain, and tRNA ferrying the next amino acid. The attachment sites are positioned so that the enlarging polypeptide chain is held between these two ribosome sub-units.

MODELING PROTEIN SYNTHESIS

Use scissors to cut out and trim each of the eight tRNA molecules on page 30. Align the anticodon of each tRNA with its appropriate codon on the mRNA strip. Use a strip of tape to attach the amino acids together. Use scissors to snip the taped chain from the attached tRNA molecules.

What is the sequence of amino acids that forms this protein chain?

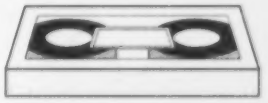
Messenger RNA


A U G C C A A G C A A A U A C G C G G U C U U A U A A
R R R

Delivering Amino Acids to Build Proteins

Objective

Students will read about the structure and function of transfer RNA; then, they will use codons and anticodons to assemble a model of a protein chain. Students will understand that tRNA uses the mRNA code to order amino acids at the ribosomes during protein synthesis.



Video Connection:
See the animation of protein synthesis.
(3:28)

Teacher Notes

Part A: Transfer RNA

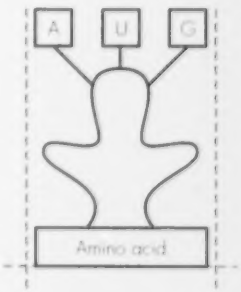
Use the codons below to help describe translation from the genetic code of nucleic acids to the amino acid sequence of protein. The uppercase letters represent nucleotide triplets. The words beneath the triplets identify the specific amino acid specified by the codon. Although each amino acid is identified by more than one codon, each codon specifies only a single amino acid or stop/start command.

Remind students that the codons are found on mRNA; the complementary anticodons are found on tRNA. Reemphasize to students that there are only four DNA nucleotides and only 20 amino acids. This is a common point of confusion for students. By varying the sequence and number of amino acids, however, these relatively small numbers of raw materials can create thousands of types of proteins.

GUC	UAC	UUU	GUA	GAA
valine	tyrosine	phenylalanine	valine	glutamic acid

Part B: Protein Synthesis

Review the concept of codon and anticodon. When cutting out the tRNA on page 30 have students trim the representation along the bottom and side margins of the amino acid name as shown at right. The amino acids can be attached by a spot of glue to the left margin of the page.



Trimming tRNA figures

Summarize to students that a healthy cell manufactures its own proteins using its DNA code. A virus takes over this process when it infects a cell to force the cell to manufacture viral proteins. HIV-infected cells make both new viruses and cellular proteins. Reemphasize that when enough cells are no longer healthy, the entire organism becomes sick (e.g., the human body). Later chapters will discuss how HIV infects and eventually kills certain human immune response cells. When these white blood cells are lost, the immune response suffers, and the person dies of infections from an assortment of microbes.

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Answers to Student Questions

Part A

1. a. Six
   b. Five, plus "stop"
   c. Start synthesis and the amino acid methionine
   d. End synthesis
   e. UACGCUUCCUUUAGUAUC
2. Methionine, valine, leucine, asparagine, lysine, valine, arginine, serine, stop.
3. a. CCA
   b. CGC
   c. UAC
   d. Methionine, begin protein manufacture

Part B

1. UACGGTTCGTTTATGCGCCAGAATATT
2. Nine
3. First codon signals the ribosome to begin manufacturing the chain. The final codon tells the ribosome to halt manufacture.
4. One
5. One
6. CAG
7. UUU, lysine

Question from margin box: Methionine (start), proline, serine, lysine, tyrosine, alanine, valine, stop

8. The code for making blueprints is stored on DNA.
   The DNA double helix "unzips."
   The DNA code is copied onto a single strand of mRNA by RNA polymerase.
   The DNA double helix "zips" closed.
   mRNA leaves the nucleus and enters the cytoplasm.
   mRNA forms a complex with a ribosome.
   tRNA attaches to an amino acid.
   Amino acids are brought to the mRNA/ribosome complex by tRNA.
   The genetic code is translated.
   Peptide bonds form between adjoining amino acids.
   The completed polypeptide chain separates from the ribosome.

Vocabulary

anticodon - the portion of the tRNA molecule that bears the complementary base triplet to the mRNA codon

codon (triplet of bases) - unit of genetic code formed by a sequence of three bases

tRNA (transfer RNA) - nucleic acid that ferries amino acids and translates the genetic code

translation - the change from a nucleic acid code to an amino acid sequence

THE FLOW OF GENETIC INFORMATION

Write the top statement (referred to as the central dogma of molecular biology) on the chalkboard. Explain that the arrows refer to the flow of genetic information. Then have students explain the statement in their own terms.

DNA → RNA → Protein synthesis

RNA → DNA → RNA → Protein synthesis

Challenge the students to describe the components required by a system in which the bottom flow of information occurs. The answer is that a virus (specifically a retrovirus, like HIV) inserts its RNA code into the cell's DNA by reverse transcription from viral RNA to DNA. Thus, in the process of the cell making its own RNA, it also makes virus specific RNA. (See Chapter Two for more details about retroviruses and HIV.)

TEACHER SUMMARY

CHAPTER TWO

The Virus

A Dangerous Piece of Information

Curriculum Connections

- Characteristics of Living Things
- Viruses and Monerans
- Plant and Animal Viruses
- The Nature of Disease

Chapter Concepts

Chapter Two introduces the virus as a non-living particle that requires the cellular machinery of a host cell to replicate itself. A virus can be categorized either by the kind of nucleic acid it contains (DNA or RNA) or by its structural and functional aspects.

The Human Immunodeficiency Virus (HIV) is a special kind of RNA virus called a retrovirus. While most viruses just insert their genetic material into a cell's cytoplasm, retroviruses convert their RNA genetic material into DNA and insert it into the DNA of the host cell. Viral code within the cell's DNA is called a provirus. The provirus is the dangerous piece of information that eventually kills the host cell after many new viruses are produced.

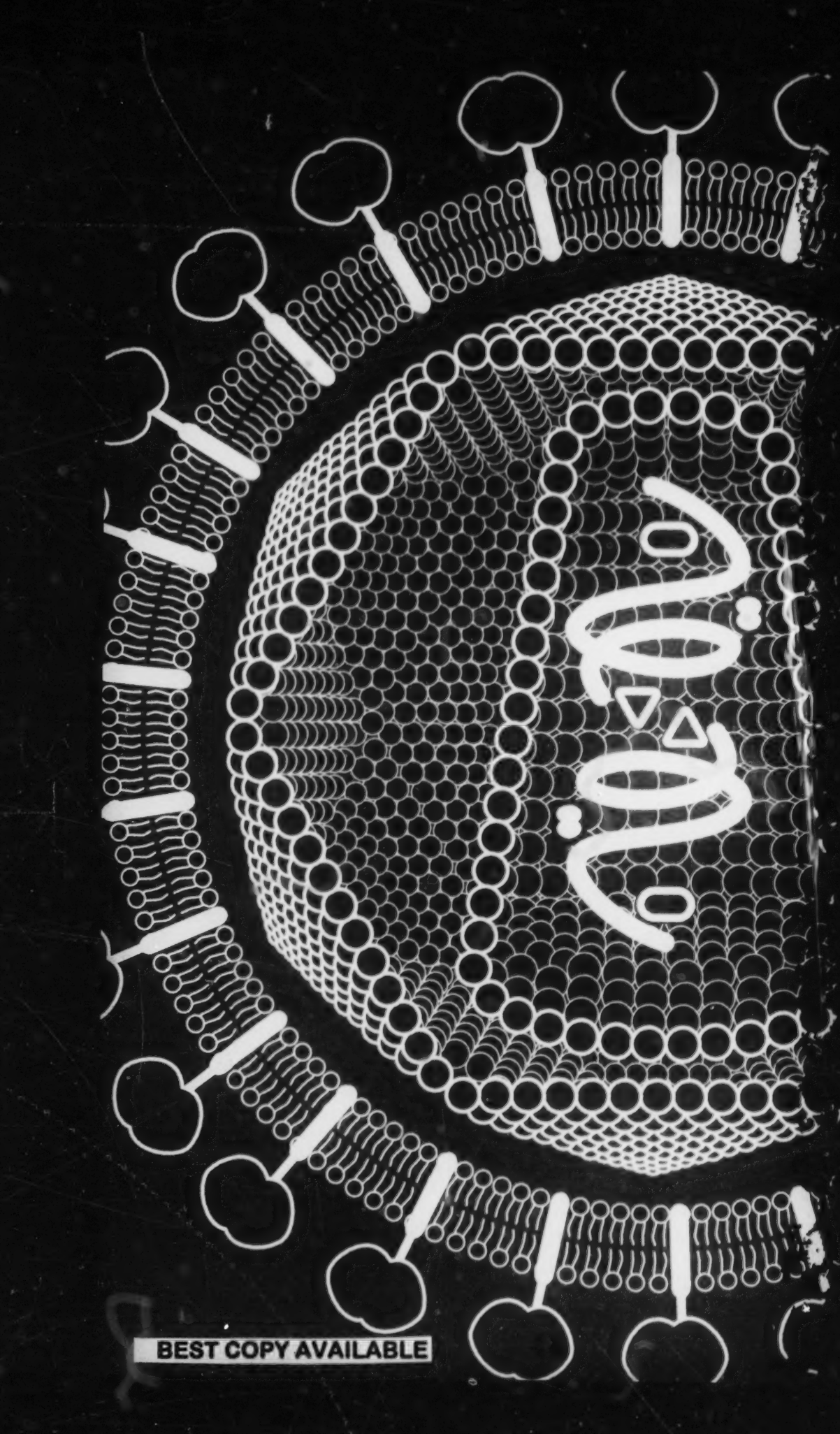
The HIV structure and replication cycle provide keys to how the virus infects human cells. The genetic code (or genome) of HIV has been completely mapped. The genes for the structural and functional parts of an HIV particle can be located on the HIV genome map. Scientists use information about how HIV replicates within the host cell to find ways to stop or reduce HIV infection.

National Science Education Standards

Content Standards 9–12

Content Standard C: The Cell; Biological Evolution; The Interdependence of Organisms

Content Standard G: History and Nature of Science; Historical Perspectives (Discovery of Viruses)



The Virus

A Dangerous Piece of Information

On the Edge of the Art: An Introduction to VR

Lab Activity: John Mosaic Virus

Viruses: Structure, Sizes, and Types

HIV Structure

HIV Replication

The Genetic Code of HIV

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On the Edge of Life

An Introduction to Viruses

Cell machinery never breaks for lunch. In fact, as long as a cell is alive, it is constantly manufacturing matter it needs to live and reproduce itself. Most of what the cell produces is protein. Protein not only repairs broken cell parts, but also provides structure and plays essential roles in the processes that keep cells alive.

Suppose something goes wrong with protein synthesis. Perhaps an intruder enters the cell and takes over the biochemical machinery. No longer does the cell produce proteins essential for its survival. Instead, it is reprogrammed to produce alien materials needed for the intruder's replication. As the cell continues on its wayward mission, it suffers. Eventually the cell rips apart, releasing a new brood of infectious particles. This is the ordinary replication cycle of a **virus**.

Viruses are different from all living things. Not only are they much smaller than the tiniest organisms, but viruses lack most of the structures found in living cells. A virus does not have a nucleus nor cytoplasm. Viruses do contain either DNA or RNA within a protective protein coat. The protein coat shelters its genetic cargo from an often hostile environment. Viruses like HIV have a lipid membrane derived from the host cell as it buds.

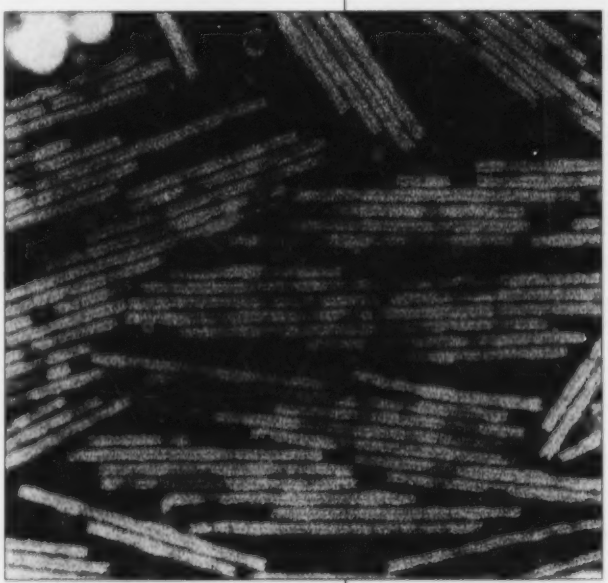
Outside a host cell, the virus is truly a non-living biological particle. It uses no energy. It performs no activities. Since the virus has no organelles, it cannot replicate by itself. It requires the cellular machinery of a host cell to make more **virions**, or mature virus particles.

THE DISCOVERY OF VIRUSES

In the late 1800s, Aldolf Mayer, a German chemist, studied the splotchy leaves of unhealthy tobacco plants. Mayer called this condition "mosaic disease of tobacco." Mayer removed the spotted leaves from the unhealthy plants. He ground them up into a liquid. Next, he injected the liquid into healthy plants. Most of these plants developed diseased leaves. From this observation, he reasoned that the disease was infectious. He could not, however, isolate the agent. Apparently, it was too small to be trapped by his filters. His experiments suggested the existence of infectious biological particles.

In 1897, a Dutch microbiologist, Martinus Beijerinck, studied tobacco mosaic disease. He observed that even when he diluted the sap from diseased plants, the liquid remained infectious (which meant that the unseen agent replicated to bring the concentration back up).

It wasn't until the 1930s that particles as small as viruses were actually seen. A new type of microscope, an electron microscope, was invented that used a beam of electrons to illuminate a universe too small to be seen with existing optical devices. In 1935, a crystallized form of **Tobacco Mosaic Virus** was examined using an electron microscope. For the first time, scientists observed that these particles, like the cells they infected, had a distinct and definite structure.

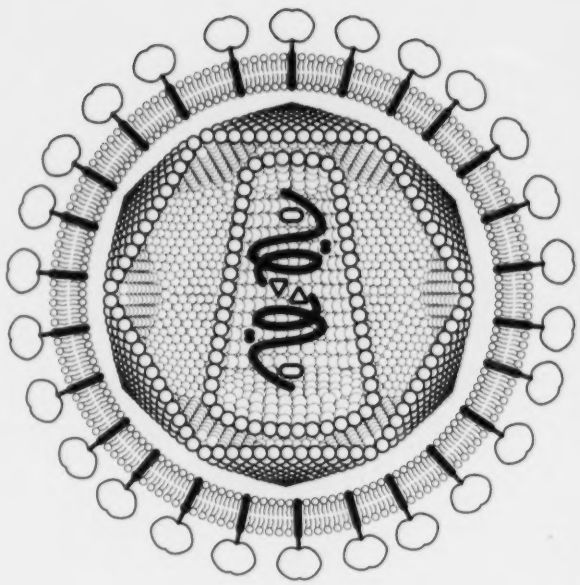


COURTESY OF DR. R.S. KIM, UNIVERSITY OF ARKANSAS

Electron micrograph of Tobacco Mosaic Virus

When a virus enters a host, it does not immediately kill the cell. Instead, it takes over. The virus reprograms the cell to make more viruses. Sometimes, new viruses are released slowly. Other times, they exit in mass. Once outside the host cell, viruses become inert again.

The **Human Immunodeficiency Virus (HIV)** is similar to many viruses. It targets and infects specific cells. The cells targeted by HIV are the body's immune cells. But unlike some viruses, HIV shares the protein machinery with the cell and doesn't immediately kill the cell as new virions bud from the cell. Eventually, HIV-infected cells die, but we don't yet know why. The death of HIV-infected immune cells hurts the body's ability to fight microbes. Over time, an HIV infection progresses to its most severe form, AIDS, or **Acquired Immune Deficiency Syndrome**. AIDS is diagnosed when patients have a defined immune cell count or when they have certain illnesses.



HIV

Questions

1. Complete the following chart. Place a mark in the appropriate box that identifies the structures/capabilities associated with cells and viruses.

STRUCTURE/CAPABILITY	CELL		VIRUS	
	present	absent	present	absent
Contains:				
Nucleic acid	☐	☐	☐	☐
Ribosomes	☐	☐	☐	☐
Proteins	☐	☐	☐	☐
Nucleus	☐	☐	☐	☐
Endoplasmic reticulum	☐	☐	☐	☐
	yes	no	yes	no
Replicates	☐	☐	☐	☐
Manufactures protein	☐	☐	☐	☐
Manufactures nucleic acid	☐	☐	☐	☐
Can be seen by optical microscope	☐	☐	☐	☐
Can be seen by electron microscope	☐	☐	☐	☐

2. What two substances do viruses contain?
3. Suppose a sub-cellular agent was causing a disorder in apple trees. Design an experiment that would distinguish the agent as a virus or a poison.
4. Are viruses living? Explain.

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On the Edge of Life

An Introduction to Viruses

Objective

Students will read and compare structures and functions of cells and viruses. Students will understand that viruses exist in a quasi-living state. Although they replicate, viruses do not have cell organization or structure. Outside of a host, viruses are lifeless.

Teacher Notes

Review the characteristics that distinguish the living condition from the non-living condition. Have students discuss the classification of a virus as a living or non-living entity.

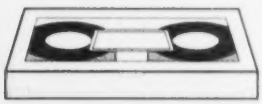
Explain that the word *virus* is the Latin word for poison. Until the 1930s, all harmful agents small enough to pass through a bacterial filter were called viruses. This included both toxins and viruses.

Emphasize the limited abilities of viruses, then draw a comparison back to the many abilities of cells. Finding treatments for HIV infection is difficult because viruses use the cellular machinery to replicate. It is difficult to stop virus replication without toxic effects to the host cell. In the section on HIV replication, students will be given an opportunity to think up ways to "interrupt" HIV, and thus inhibit HIV infection.

Discuss the scientific method. Describe systematized testing that is applied to understanding the natural world. Have students brainstorm a variety of questions about viruses. Challenge student groups to develop experimental designs that would generate the answers to selected questions.

EVOLUTIONARY ORIGINS OF VIRUSES

There are three major theories about the origin of viruses. The first theory proposes that viruses arose from cells that progressively lost both cellular machinery and genetic information. Soon these dwindling cells were reduced to total dependence upon host cells. The second theory proposes that viruses arose directly from the genetic material of host cells. Bits of replicating nucleic acid broke from the host chromosomes. These bits evolved into obligate parasites. The third theory treats viruses as complex polymers that arose at the same evolutionary time as other cellular molecules.



Video Connection:
See the first part of the video for an introduction to viruses.

Answers to Student Questions

1. Comparison of cells and viruses

STRUCTURE/CAPABILITY	CELL		VIRUS	
	present	absent	present	absent
Contains:				
Nucleic acid	■		■	
Ribosomes	■			■
Proteins	■		■	
Nucleus	■			■
Endoplasmic reticulum	■			■
	yes	no	yes	no
Replicates	■		■	
Manufactures protein	■			■
Manufactures nucleic acid	■			■
Can be seen by optical microscope	■			■
Can be seen by electron microscope	■		■	

2. Protein and nucleic acid
3. Dilute the suspected agent and observe whether it retains or loses its ability to infect healthy trees.
4. They exist in a quasi-living state. Although viruses replicate, they do not have cell organization or structure. Outside of a host, viruses are lifeless.

Vocabulary

Acquired Immune Deficiency Syndrome (AIDS) - a collection of disease symptoms that appear in the most severe stage of HIV infection

Human Immunodeficiency Virus (HIV) - produces a compromised immune response; over time the HIV infection progresses to AIDS

Tobacco Mosaic Virus (TMV) - a virus whose attack on tobacco and other plants produces a mottled leaf appearance

virion - complete or mature virus particle

virus - non-living, obligate parasite consisting of nucleic acid and a protein shell

Lab Activity

Tobacco Mosaic Virus

Tobacco mosaic disease is an infectious disorder caused by the tobacco mosaic virus which can infect a limited variety of plants. Since it cannot infect humans or other animals, it is a safe virus for investigation. When TMV infects a **pinto bean plant**, it spreads only within the cells of leaves onto which it is applied. As the virus replicates, it destroys tissue. In this activity, you'll observe leaves of both healthy and infected pinto bean plants. Then you will transfer the virus onto a healthy plant and observe the effects of infection.

Materials

- healthy bean leaf
- healthy pinto bean plant
- pinto bean plant infected with TMV
- TMV solution
- marker
- diatomaceous earth
- sterile cotton swabs
- distilled water
- spray bottle

Steps

1. Examine the leaves of healthy and TMV-infected plants. Sketch and record the appearance of the leaves.
2. Gently brush the surface of two healthy pinto bean leaves with **diatomaceous earth**. Mark the plant container to distinguish the leaves.
3. Use a sterile swab to gently "paint" the TMV solution onto the surface of one leaf that has been brushed with diatomaceous earth.
4. Use another sterile swab to "paint" a drop of distilled water onto the brushed surface of the other leaf.
5. Spray the leaves with a mist of distilled water. Let dry. Set the plant aside in a place identified by your instructor.
6. Wash your hands to prevent transferring the virus out of the lab.
7. Prepare a chart for observations of the leaves. Record daily.

Questions

1. What happened to the leaves that were treated with TMV solution?

2. What happened to the leaves that were treated with distilled water?

3. What was the purpose of treating leaves with water?

4. How did the diseased leaves that you produced compare with the leaves you examined at the beginning of this activity?

Think About It

How could you use an extract from the diseased leaves to demonstrate the infectious nature of TMV?

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Lab Activity

Tobacco Mosaic Virus

Objective

Students will conduct a hands-on experience in viral biology to understand general principles of viral infection.

Teacher Notes

Review the role of TMV in the discovery of viruses (see page 36). Explain that this virus targets the cells of tobacco plants and the cells of "hypersensitive hosts," such as a pinto bean plant. Within a host, TMV does not spread beyond the leaf to which it is applied.

Preparation (two to three weeks)

You'll need to grow a classroom set of pinto bean plants (*Phaseolus vulgaris*). The beans are readily available at local food markets. Once planted, the seedlings will grow to appropriate size within two weeks. You may wish to infect several plants a few days earlier. This will verify the infectivity of the TMV.

TMV Sources

You can obtain TMV from a variety of sources including Carolina Biological Supply Company, 2700 York Road, Burlington, NC 27215, (800)334-5551; or the American Type Culture Collection, (800) 638-6597.

Safety

Remind students that TMV cannot infect humans or other animals. Since TMV can be transferred to plants outside of the laboratory, it is critical that students follow sterile techniques and wash up after the activity.

Extending the Activity

Have students create an experimental design that can test:

a. the effectiveness of brushing leaves with diatomaceous earth
b. if boiling or freezing inactivates TMV
c. if other plants also can be infected by TMV
d. if the virus passes through a set of classroom laboratory filters

Vocabulary

diatomaceous earth - a fine abrasive material consisting of microscopic diatom shells

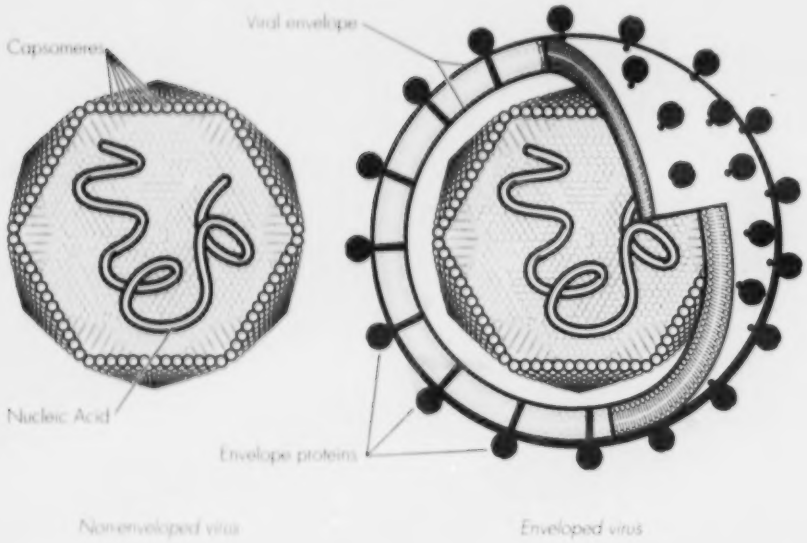
pinto bean plant - an easily maintained plant that is a hypersensitive host of TMV infection

Viruses

Structures, Sizes, and Types

Part A: Virus Structure

Perhaps you've examined a clam or snail. If so, you know that these animals are protected by a rock-hard shell. This protective capsule shelters the animal's soft parts against the ravages of weather, chemicals, and hungry predators.



The genetic code of viruses is also safeguarded by a protective capsule called a **capsid**. Capsids are rigid protein shells that have several different shapes. Some capsids, such as those of the tobacco mosaic virus, are shaped like a thin rod. Other capsids have a much rounder shape. A common capsid shape is formed by 20 triangular sides, called an **icosahedron**.

Since a capsid is too large to be formed by a single protein molecule, it is constructed from smaller building blocks. These subunits are called **capsomeres**.

Building a capsid from capsomeres saves genetic material. If the same unit is repeated, fewer genetic blueprints are needed. Repetition of units offers another advantage. Suppose one brick in a huge wall were misshapen. By sheer numbers, the remaining bricks would keep the wall in place. In a similar way, the use of repetitive capsomeres offers a type of "integrity" insurance.

TEM COURTESY OF A. HARRISON, CDC

HIV budding from infected T cell (a white blood cell)

Some viruses have capsids that are surrounded by an outer cloak called a **viral envelope**. This covering is mostly made of pieces of cell membrane, picked up as the virus buds out of the host cell. The viral envelope also contains proteins from the viral blueprint that can connect with certain receptor proteins on target cells. When the virus protein and the host cell receptor protein connect, like a lock and a key, the virus can enter the cell to take over. In this way, the viral envelope proteins help these kinds of viruses enter specific host cells. HIV is an example of a virus that has a viral envelope. HIV has a protein in its envelope that binds with a receptor (called **CD4**) on certain kinds of white blood cells in the human body. HIV can infect cells that have the CD4 receptor on their surface.

Both the capsomeres and envelope proteins are made by the infected host cell using the genetic information from the virus. Once reprogrammed, the cell's ribosomes produce long strands of viral proteins. Often these strands contain a chain of several attached proteins. Special chemicals called **proteases** act like scissors, cutting up the strand into useful lengths. Without proteases, uncut protein chains could not be used to build new virus particles.

Questions

1. Describe two advantages of building a protein shell out of capsomeres.

2. If a virus cannot build lipid, how can the viral envelope contain this substance?

3. How would the action of a protease-blocking chemical affect viral replication?

4. How would the action of a cloaking chemical (one that binds with viral envelope proteins) affect the ability of a virus to infect a cell?

Part B: Relative Sizes of Viruses and Host Cells

Take a look at the period at the end of this sentence. In human terms, it may not be very big. However, in the minuscule world of the virus, it is a virtual cityscape! Over 5,000 tobacco mosaic viruses (TMV) can fit end-to-end across that mark's widest part.

Most viruses are smaller than TMV. In fact, the tiniest viruses are about the size of a single ribosome in a cell. A few viruses are bigger than TMV. Vaccinia, the virus that causes a disease in cows, is a giant among viruses; but vaccinia particles are still too small to be observed with an optical microscope.

How does HIV measure up? In the language of the laboratory, HIV is about 100 nm (**nanometers**) in diameter. That's about five times the diameter of a ribosome. The target of HIV attack is a white blood cell. The white blood cell is huge when compared to HIV. If HIV were the size of a softball, its host cell would be about the size of a classroom.

SEM COURTESY OF C.S. GOLDSMITH, CDC

T cell infected with HIV (for size comparison)

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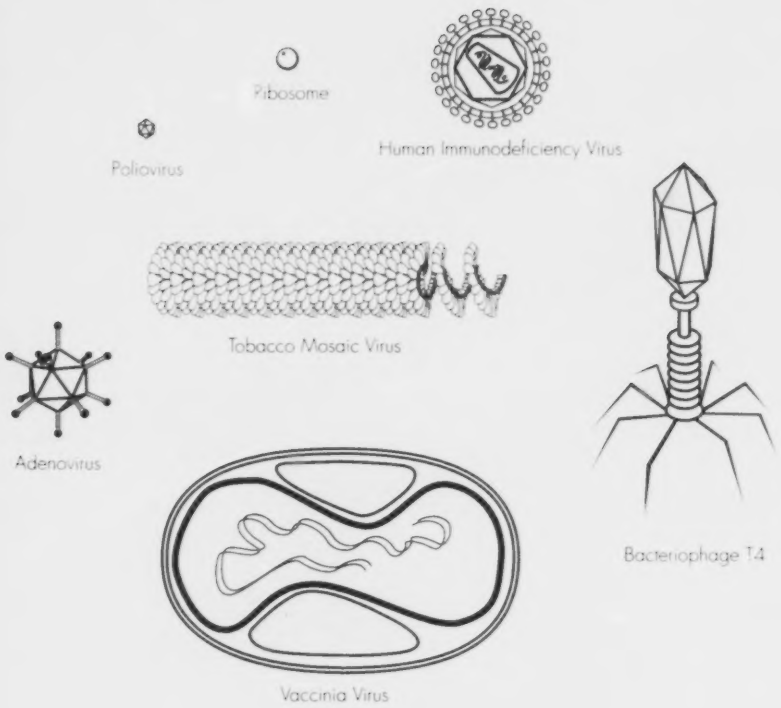


Questions

Examine the viruses at left.
Use a ruler to determine the approximate dimensions of each particle. Scale: 1 mm equals about 6 nm (nanometers).

Adenovirus _____

Bacteriophage T4 _____

Human Immunodeficiency Virus _____

Poliovirus _____

Vaccinia _____

Tobacco Mosaic Virus _____

Ribosome (cell organelle) _____

Part C: Virus Types

Suppose you were asked to categorize things that you couldn't see. What would you base your classification upon? Up until the 1930s, biologists embraced the *you are what you infect* scheme. Viruses, although unseen, were classified into one of three groups by what they infected—plant viruses, animal viruses, and bacterial viruses. Although this method of grouping was useful, it produced limited and sometimes dubious associations. Virus particles with different structures, different methods of infection, even different genetic material (RNA or DNA) were placed in the same group.

Today, we have a broader classification scheme. Although the host-based categories can be useful, viruses are grouped also by their nucleic acid content.

DNA Viruses

DNA viruses contain either a single strand or paired strand of DNA. When a DNA virus infects a cell, its genetic code is copied into viral mRNA. The mRNA travels to the host ribosome. At the ribosome, the viral mRNA directs the manufacture of proteins essential for the parasite's replication.

RNA Viruses

Other viruses, such as TMV and poliovirus, contain RNA. Once the virus infects the cell and releases its RNA, the RNA is.a "ready-made" code that attaches to the host ribosomes. There it is changed into virus proteins. But there is a special kind of RNA virus which replicates in a different manner.

HIV: A Retrovirus

In the 1970s, the discovery of the enzyme **reverse transcriptase** confirmed the existence of a unique class of RNA viruses. These viruses were called **retroviruses.** Their name reflects a unique mode of replication.

Within the HIV-infected host cell, genetic information flows from the retrovirus in the reverse direction. Reverse transcriptase converts viral RNA to viral DNA. This change from RNA to DNA occurs in no other living system. Next, the viral DNA inserts itself into the host chromosome. From the safety of the cell nucleus, the viral blueprints are copied as if they were the host's own genetic code.

Until several decades ago, retroviruses were mostly a laboratory curiosity. In the early 1980s, HIV was isolated in patients that were suffering from severe immune deficiency. Studies confirmed that infection by this retrovirus progressed to AIDS.

Questions

This table presents information that describes several viruses. Use this information and what you have already learned about viruses to answer the following questions.

VIRUS	NUCLEIC ACID	STRUCTURE	HOST
HIV	single strand RNA	capsid and viral envelope	animal
Adenovirus	double strand DNA	icosahedron capsid	animal
Vaccinia	double strand DNA	capsid and viral envelope	animal
TMV	single strand RNA	helical rod capsid	plant
Poliovirus	single strand RNA	icosahedron capsid	animal

1. Which of the above viruses has a capsid formed from 20 identical triangular capsomeres?

2. Which of the above viruses contains membrane picked up as the virus leaves the host cell?

3. Which one of the above viruses inserts its code into its host's DNA?

Viruses

Structures, Sizes, and Types

Objective

Students will examine viral structure in terms of the complete virus and its component parts. Students will compare the different sizes of example viruses, and the size of HIV compared to its host cell. They will understand that there are two basic virus types (based on what kind of nucleic acid they contain): DNA and RNA. An important point is that HIV is a retrovirus, a special kind of RNA virus.

Teacher Notes

Part A: Virus Structure

Compare and contrast clam shells with viral capsids. How are they different? How are they alike? Discuss the consequences of exposing a fragile material (such as nucleic acid) to the environment. Have students identify heat, UV radiation, and corrosive substances as factors that might damage the structure of this substance.

The formation of viral envelopes can be demonstrated by blowing bubbles using soap solution. Explain that the bubble is like the cell membrane that surrounds the viral material as it pushes out from the cell. As the bubble floats in the air, it is a representation of a newly budded virus—free from the host cell, but built from material that came from the host cell (the soap solution).

BACTERIOPHAGES

Bacteria-eating viruses were first discovered in 1915. Their presence was inferred from the sudden and rapid death of bacterial cultures. In the 1940s, bacteriophages became a preferred tool of biochemists. Their ability to transfer nucleic acid was essential to developing the foundations of molecular biology.

Part B: Relative Sizes of Viruses and Host Cells

Compare and contrast the relative sizes and shapes of different viruses. The cover of this book shows a T cell with small blue HIV virions. Use that photo and the photo on page 43 to convey scale. How can an infective virus (of ribosome size) contain enough parts to replicate? Answer: it doesn't; a virus usually contains only nucleic acid and protein, and uses the host cell to manufacture viral proteins.

The following information is background about each of the viruses illustrated on page 44.

Human Immunodeficiency Virus (HIV) - virus that produces a compromised immune response in humans; over time the HIV infection progresses to AIDS

Bacteriophage T4 - virus that targets bacterial cells

Adenovirus - infects tonsils and adenoid glands in humans; causes respiratory disease

Vaccinia - relatively large, brick-shaped virus that produces cowpox; infection with vaccinia produces immunity to smallpox in humans

Tobacco Mosaic Virus (TMV) - rod-shaped virus that produces a mottled-leaf disorder in tobacco and other plants

Poliovirus - relatively small virus that causes infantile paralysis in humans

As an art extension, supply the class with chalk, meter sticks, and page 44. Have student groups use the relative sizes to create "large-scale" sidewalk art of these viruses.

Part C: Virus Types

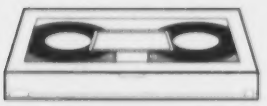
To teach about retroviruses, write the following flow diagram on the chalkboard. Review how this diagram describes the normal flow of genetic information.

DNA → RNA → Protein synthesis

Write the following flow diagram on the chalkboard. Explain how this flow of information begins with a step that is found only in retrovirus replication.

RNA → DNA → RNA → Protein synthesis

In no other system does genetic information flow from RNA to DNA. Have students discuss the significance of integrating the viral code into the host DNA. Inserting viral code directly into host DNA means that the viral code can never be removed by the cell. The extra step of replication from RNA to DNA makes retroviruses, particularly HIV, susceptible to many errors in replication. This can be an advantage for either the host or the virus. For example, mutations during replication of HIV can either result in viruses that are more virulent or less virulent than the original virus. It is difficult to find a "cure" for HIV because: (a) once infected, a host cell (or any drugs developed so far) cannot remove the HIV DNA; and (b) HIV mutates so frequently that drug developers must play catch up with the virus in developing new drugs. Multi-drug therapy is proving to be a useful regimen for addressing the later problem. See Chapter Five for more information.



Video Connection:
See animations of DNA replication and RNA replication for an explanation of mutations. (22:20)

Answers to Student Questions

Part A

1. Less genetic code is required. Since there are many, a single flawed one will probably not have an effect.
2. The lipid is torn from the host membrane as the virus exits the cell.
3. The long "polyprotein" strands could not be cut into functional proteins, and thus new virions would be incomplete (not able to infect new cells).
4. The virus could not enter or infect the host cell.

Part B

Measurements of:

Adenovirus	~75 nm
Bacteriophage T4	~65 nm across head, 300 nm tall
Human Immunodeficiency Virus	~100 nm
Poliovirus	~18 nm
Vaccinia	~300 nm long
Tobacco Mosaic Virus	~300 nm long
Ribosome	~20 nm

Part C

1. Adenovirus and poliovirus
2. HIV and vaccinia
3. HIV

Vocabulary

capsid - a protein shell of a virus containing nucleic acid

capsomere - the protein "building-block" of a capsid

CD4 - a protein complex found on the surface of cells that HIV can infect

icosahedron - a geometric shape formed by 20 triangular sides

nanometer (nm) - a unit of measurement equal to 10^{-9} meters

proteases - the enzymes that are required to cleave polypeptide chains into smaller, functional units

retroviruses - a group of viruses whose replication cycle involves the transfer of RNA code to DNA

reverse transcriptase - the enzyme that accelerates the transcription of RNA code into DNA

viral envelope - the outer viral covering formed by the host membrane and viral protein studs

HIV Structure

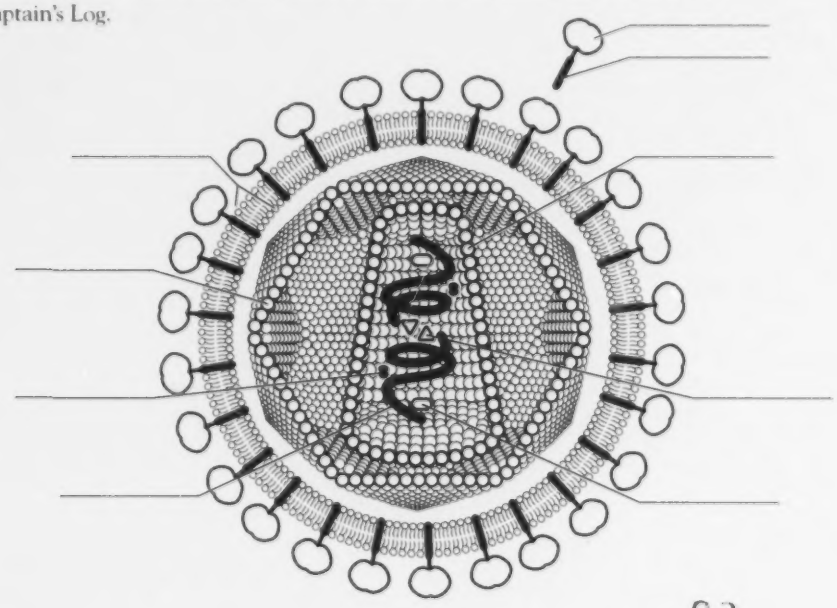
Suppose you were in a submarine with a crew of scientists reduced to microscopic size and injected into the bloodstream of a normal-sized person. Racing against time, the team maneuvers through the man's body in a desperate effort to relieve a blood clot that has formed on his brain. Within their extraordinary surroundings, the crew observes and interacts with the body at a cellular level.

Imagine this miniaturized world. What would you see? The following Captain's Log is a report of just such a voyage as a miniaturized research team observes a Human Immunodeficiency Virus.

As you read the log, use this chart to make your own record of the voyage by taking notes on what the crew observed.

COMPONENT	DESCRIPTION	LOCATION	FUNCTION
gp120			
gp41			
p17			
p24			
RNA			
reverse transcriptase			
protease			
integrase			

Identify the structures illustrated on the following diagram as described by the Captain's Log.



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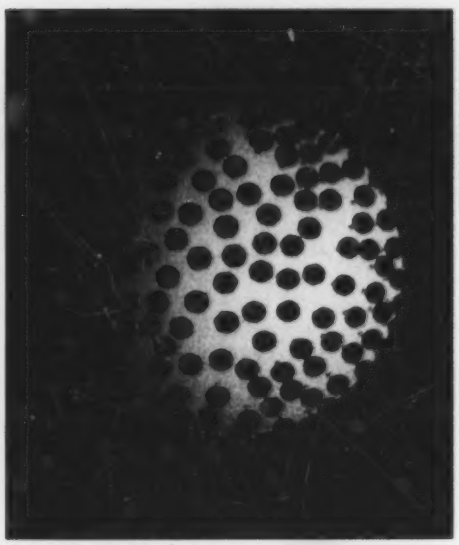
This was a landmark day for science. For the first time, we were able to view HIV close-up without the filters imposed by a microscope.

The miniaturization went smoothly. The process is directly the opposite of what many people might expect. My crew and I didn't feel like we were getting smaller; instead, everything around us appeared to grow to an immense size. Within 10 minutes, our submarine was shrunk to one-tenth the size of an HIV particle.

The reactions of my crew were priceless. Jane Boyington, our epidemiologist from the National Institutes of Health, and Bob Doran, the virologist from Cornell University, had their noses pressed up against the window the entire time. They just loved it. Neil Walker, who ran the robotic systems, closed his eyes and dug his fingers into the arm rests of his seat. I think it will be a while before he volunteers for another mission like this one.

After the miniaturization was completed, our craft was lowered into a test tube that harbored the virus. Neil and I powered up the submarine and began our search for a virus particle. We had placed bets on who would be the first to spot one. Jane won; about five minutes into the mission, she spied a particle off the port bow.



COURTESY OF P. FELDMAN, NIH

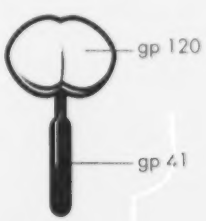
Computer model of HIV

From a distance, the single HIV, called a virion, appeared round. As our craft circled the membrane's outermost boundary, we observed the presence of small particles. Some of the particles were embedded into its fabric. Others extended beyond the membrane surface and projected outward.

Neil used a robotic scoop to sample both the membrane fabric and the assortment of attached particles. Bob's analysis showed that the fabric of this outer cloak was made of a lipid. Many of the embedded particles were proteins and sugar complexes that were not of viral origin. Apparently, this membrane along with some cell markers, were torn from the host cell during the budding process.

Jane suggested that we focus our attention on a specific marker that studded the entire envelope surface. Chemical analysis revealed that the stud was made up of sugar and protein. This mixture of materials is called a **glycoprotein**. *We only saw it on HIV and the membranes of HIV-infected cells.*

Further examination revealed that the stud was formed by two attached parts. The upper cup-like part extended from the envelope. The mass of this part was equal to the mass of 120,000 hydrogen atoms. Based on this mass and composition, we named it **glycoprotein 120**, *or simply* **gp120**. *The base of each gp120 was attached to another glycoprotein. This smaller part was anchored in the envelope membrane. Although it was also made of glycoprotein, this transmembrane part had a mass of only 41,000 hydrogen atoms. We called it* **gp41**.

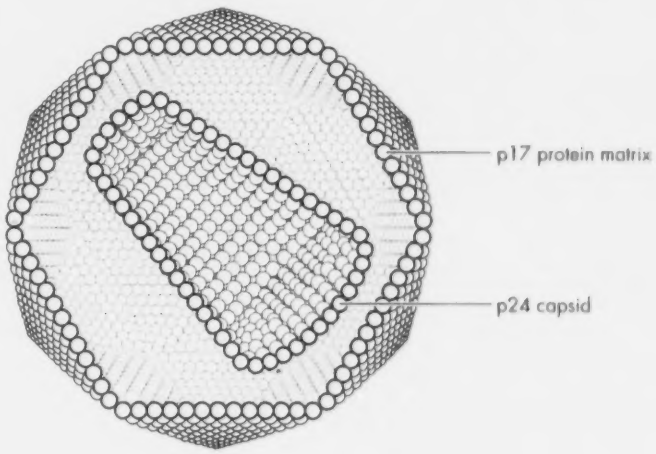


A debate ensued over whether or not we should enter the virion. Jane and Bob, thrilled with being able to study the virus in three dimensions for the first time, pressed to continue our voyage of discovery. Neil and I both had concerns over how enzymes within the virus could affect the submarine's systems. After consulting with Mission Control, which reassured us that the risks were minimal, I agreed to press forward.

With the engines on full throttle, we passed through the soft lipid envelope. Just beneath its surface, we encountered a stiff structural cage. This large cavity was formed by a pattern of side-by-side protein building blocks. Analysis identified this as matrix protein, ***p17****.*

Within this hollow, we discovered a smaller, cone-shaped capsid. Sampling of the capsid revealed that this structure was formed by a capsomere called ***p24****. Several other proteins reinforced this inner capsid's structure.*

As we scanned the contents of this inner core, we observed two strands of RNA. Each strand contained the genetic code of HIV. Each of the strands was attached to a molecule of ***reverse transcriptase****. Earlier on in the lab, we had determined that when HIV entered a cell this enzyme helped transcribe the code from RNA to DNA. Reverse transcriptase must make many errors as it replicates new HIV DNA from the viral RNA because almost every new HIV has a mutation.*



Reverse transcriptase wasn't the only enzyme safeguarded within this inner capsid. Our probes detected both ***protease*** *and* ***integrase****. In an infected cell protease acts like chemical scissors, cutting viral proteins into usable lengths. Integrase inserts the viral code into the host's DNA. Without the action of integrase, the viral code could never become part of the cell's chromosome.*

Jane and Bob could have easily stayed here for weeks studying the virus, but I was soon ready to go home. The dark red blood, so different from the blue sea, becomes a rather unnerving environment to be in after about two hours. I eased the submarine out of the virus and then radioed Mission Control to extract us from the test tube. The de-miniaturization process went smoothly, and within 10 minutes we were back to normal.

I hope this will be the first of many medical missions. This technology could revolutionize the fields of immunology and virology.

A Model of HIV

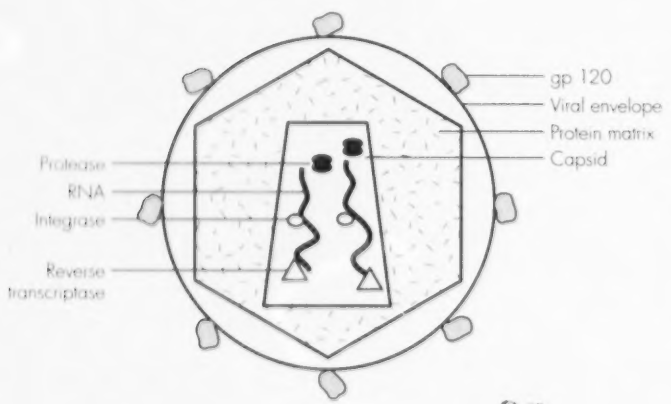
If you were a crew member of the miniaturized ship, you would be able to construct a three-dimensional model of HIV. Here's a chance to put together what you know about the structure of HIV. You will construct a model that represents an HIV virion sliced in half.

Materials

aluminum foil
protein patterns (pg. 53) copied or pasted onto heavy stock paper
scissors
clay (5 colors)
tape
hard rubber ball (tennis ball size)

Steps

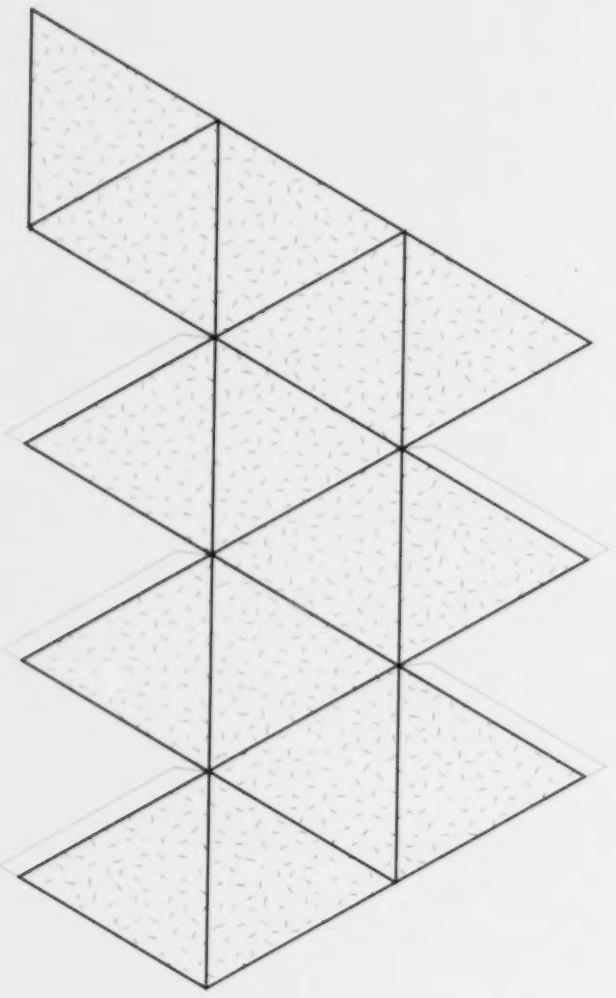
1. Tear off two squares of aluminum foil about 10 cm by 10 cm.
2. Sandwich the squares into a 3-layer thickness.
3. Wrap this thickened foil around one hemisphere of a hard rubber ball. Press out the foil, so that it forms a smooth copy of half of the ball's curved surface.
4. Break off about a dozen small lumps of clay, each about the size of a nail head. Distribute the lumps evenly across the foil hemisphere. Press the clay so that it adheres to the exposed surface.
5. Use scissors to carefully cut out the protein patterns. Score and fold the patterns into half-section representations of the protein matrix and capsid shell.
6. Roll out two spaghetti-sized lengths of clay, each about 2 cm long.
7. Mold small pea-sized balls of clay. Use different colors or shapes to represent:
   2 molecules of reverse transcriptase
   2 molecules of viral protease
   2 molecules of integrase
8. Assemble the individual parts into a model representing one half of the HIV virion.



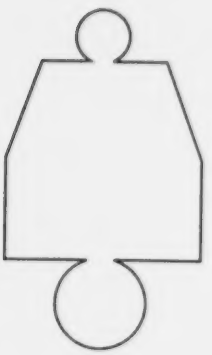
Compare and contrast your model of HIV with a real HIV particle.

65

p17 Protein matrix



p24 Inner capsid



HIV Structure

Objective

Students will learn the structural elements of HIV by reading a fictional account of a miniaturized ship passing by an HIV virion. Students will make a model of HIV to demonstrate their knowledge.

Teacher Notes

Review the complexity of the HIV particle. Use page 65 as an overhead master. After students have taken notes on the information in the Captain's Log, have them identify and describe the subunits that compose each of HIV's structural elements.

Important Point: HIV is categorized as a "single-strand RNA virus" (see page 45). However, HIV contains two identical copies of the (single) RNA strand. Therefore, the Captain's Log states, "As we scanned the contents of this inner core, we observed two strands of RNA. Each strand contained the genetic code of HIV."

HIV COMPONENT	DESCRIPTION	LOCATION	FUNCTION
gp120	cup-like projection	surface of envelope	binds to CD4 receptor
gp41	transmembrane anchor for gp120	within lipid bilayer protein	anchors the gp120 projection
p17	matrix protein	protein matrix cage	structural building block
p24	protein capsomere	capsid or "core" protein	structural building block
RNA	nucleic acid	within capsid	carries viral genome
reverse transcriptase	enzyme	within capsid	translates RNA to DNA*
protease	enzyme	within capsid	cleaves polypeptides into functional proteins
integrase	enzyme	within capsid	splices viral DNA with host DNA

**Reverse transcriptase makes many errors, perhaps every time it replicates viral RNA to DNA. These errors are the result of transcribing HIV RNA to DNA. This is one reason HIV mutates so often, and why creating a vaccine for HIV is so difficult.*

Vocabulary

glycoprotein - macromolecule consisting of a sugar and protein complex

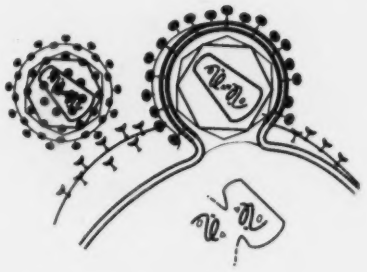
HIV Replication

Cell membranes are usually formidable barriers that keep out both harmful chemicals and microbes. However, HIV has little trouble penetrating the membranes of its target cells. HIV replicates in a multi-step process.

1. Binding and Entry of Virus

HIV penetrates the membrane of its target cells because of the binding that occurs between the virus envelope and the surface of the cell membrane. Like most viruses, HIV targets only certain cell types. All potential HIV hosts must bear the protein complex called **CD4** on the outer surface of their cell membranes. This biochemical barcode is one key to infection.

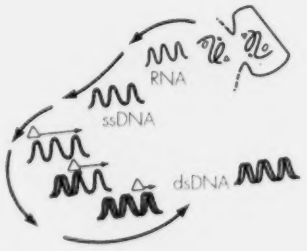
When HIV encounters a cell displaying CD4 proteins, the protein gp120 on the viral envelope locks on to the CD4 protein. The cell membrane and viral envelope fuse forming a passageway into the cell's cytoplasm. Stripped of its cloak, the viral core and contents enter the cell's cytoplasm.



1 *Binding and entry of virus*

2. RNA to DNA

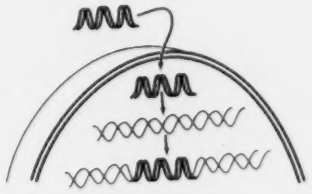
The viral reverse transcriptase then copies the single strand of viral RNA into a single strand of DNA. Then reverse transcriptase makes a second DNA strand complementary to the first. This double strand of viral DNA migrates into the cell's nucleus.



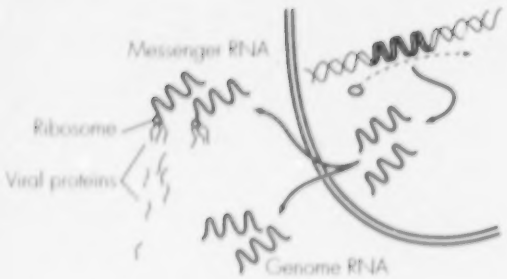
2 *RNA to DNA*

3. Integration of Viral DNA

In the nucleus, the viral enzyme integrase goes to work producing a gap in the host DNA into which the viral DNA can be spliced. Once embedded into the host chromosome, the viral genes (now called a **provirus**) provide codes for the viral protein manufacture. The activity of HIV is regulated by several of its component genes in the provirus. At first, these genes suppress the manufacture of new particles.



3 *Integration of viral DNA*



4 & 5 *Making virus RNA and virus proteins*

4. Making Virus RNA

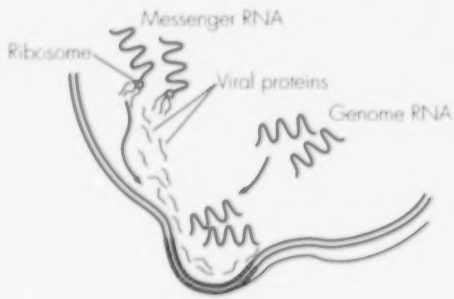
When the genes switch on, however, the HIV code is expressed. Viral mRNA is transcribed from the DNA provirus template. Some of the mRNA strands direct the ribosomes in the synthesis of viral proteins. Other segments of viral mRNA will be used as the genetic cargo of the new HIV particles.

5. Making Virus Proteins

During this takeover, the cell makes both viral and cellular proteins. The ribosomes manufacture protein according to both cell and virus blueprints.

6. Budding of New Viruses

The particles assembled from the viral proteins and mRNA are neither complete nor infectious. As they bud from the host cell, each particle tears off a section of the host membrane. This membrane surrounds the HIV capsid forming an envelope.



6 *Budding of new viruses*

7. Final Assembly of Viruses

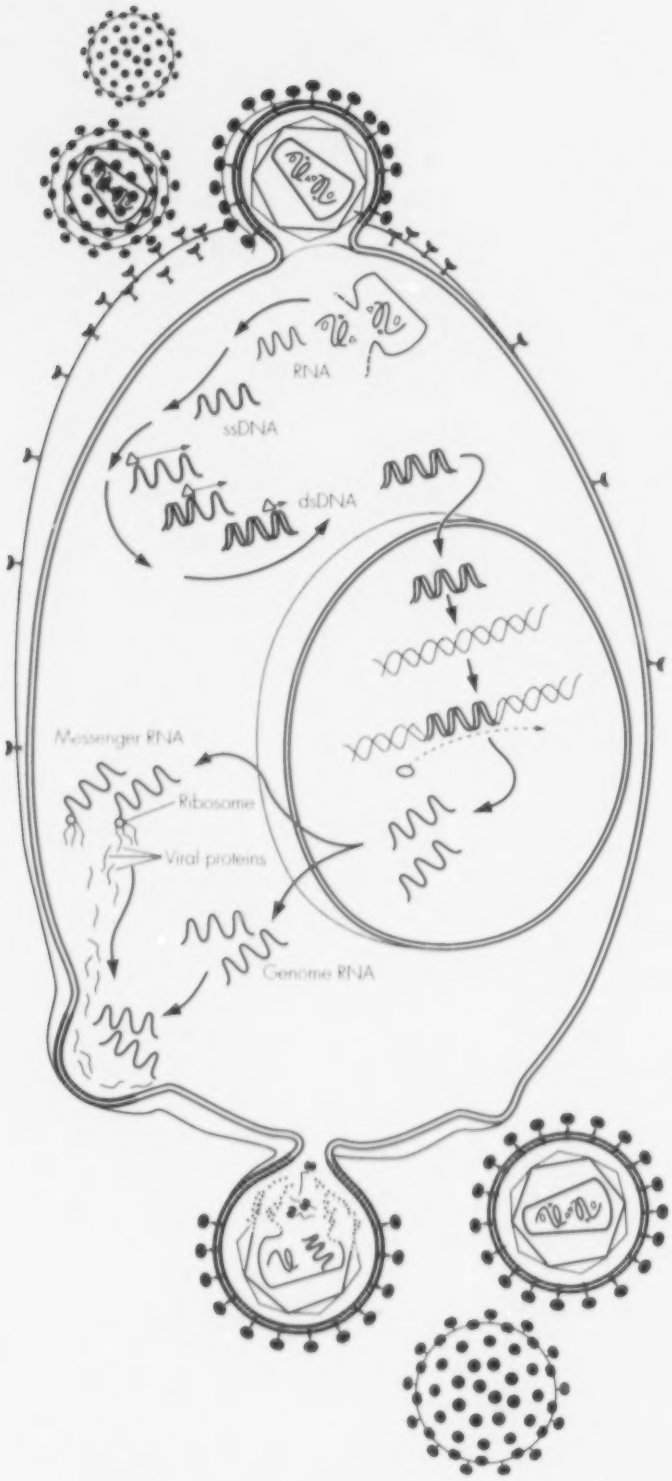
The viral protease goes to work as the HIV buds and after it is free of the cell. It cleaves some of the large viral polypeptides into p24, p17, and the three enzymes. These reactions modify the particle into an infectious virus.

7 *Final assembly of viruses*

Consider the stages of HIV replication illustrated on page 57. What could be done in each step to inhibit the HIV from completing the action? For example, what could be done to keep HIV from entering the cell in the first place?

Scientists consider this same problem as they seek treatments for HIV infection. Perhaps you can come up with some of the same answers as the scientists.

69



HIV replication

HIV Replication

Objective

Students will study the steps in the replication cycle of HIV to predict ways scientists treat HIV infection.

Teacher Notes

Use page 57 as an overhead master. Write the following names of key HIV components on the chalkboard:

RNA, reverse transcriptase, viral protease, viral integrase.

Explain that all four molecules are found within the capsid of HIV. Have students discuss the activity of each molecule, independent of its role in the replication cycle.

To illustrate the role of the protease enzyme, display a necklace of pop beads. Explain that the necklace represents a polypeptide produced by a virus infected cell. This chain, however, is too long to be used by the virus. In order to produce functional peptides, it must be cleaved into smaller units. The precision breakdown of this chain is performed by protease enzymes.

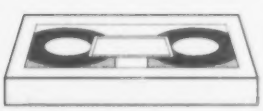
Review the concept of a provirus. Explain that the HIV provirus is the viral DNA that is inserted into the host chromosome. Integrated into the host genome, it is treated as an ordinary part of the cell's DNA. It is this inserted sequence (not the viral RNA) upon which the gene map of HIV is generated. To demonstrate, display a piece of string which will represent the host cell's DNA. Cut the string and tie a short piece of dental floss onto the (now two) pieces of string, making one long string with dental floss in the middle. The dental floss represents HIV DNA, the "provirus" in the host cell's DNA. You could also use different colors of pop beads to demonstrate this concept.

Current strategies for inhibiting HIV infection include: (a) trying to keep HIV from entering the cell; (b) trying to keep HIV from inserting its RNA into the cell's DNA; and (c) keeping protease from cutting viral proteins into useable lengths.

If you plan to teach Chapter Five, you may not want to give out these answers, but have students think about plausible strategies in preparation of Chapter Five.

PROTEASE ACTION

There are two kinds of protease: cellular and viral. Cellular protease cleaves polypeptides to form gp41 and gp120 (envelope proteins). Viral protease cleaves polypeptides during and after HIV buds from the cell to form p17, p24, and the three enzymes. See Chapter Five for a discussion of protease inhibitors used to treat HIV infection.



Video Connection:
See animation of HIV replication (8:25)

Vocabulary

CD4 - a protein complex found on the surface of cells targeted by HIV

provirus - the group of viral genes that are inserted into the host DNA

The Genetics of HIV

Part A: The HIV Genome

When scientists examine the nucleic acid blueprints of humans, they uncover tens of thousands of genes. In contrast, HIV has nine. This meager gene content (known as a **genome**) is enough to direct all aspects of the HIV's structure and function. The mechanics are supplied by the host cell.

The genetic sequence of HIV has been well analyzed and completely mapped. Some elements of the genome are strikingly similar among all HIV particles; other parts of the code vary considerably.

The RNA found in all HIV particles is comprised of about 10,000 nucleotides. These nucleotides form a linear sequence. The sequence is organized into distinct, and sometimes overlapping, sections. Each section composes a gene; each gene codes for specific proteins.

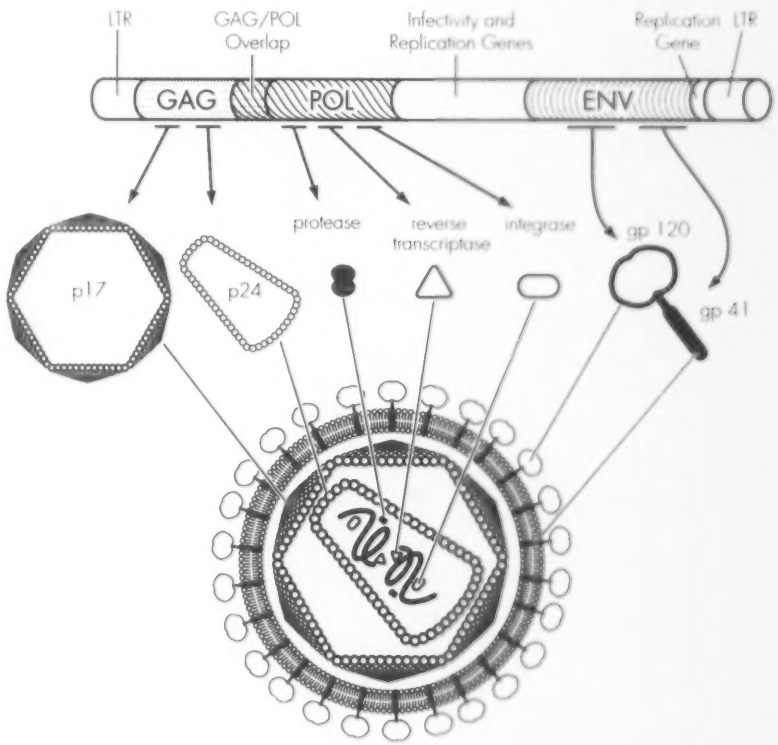
The genome of HIV contains three major structural genes called GAG, ENV, and POL.

GAG provides the code for the building blocks of p17 (matrix protein) and p24 (capsid shell).

The **ENV** gene provides the code for two envelope glycoproteins, gp120 and gp41.

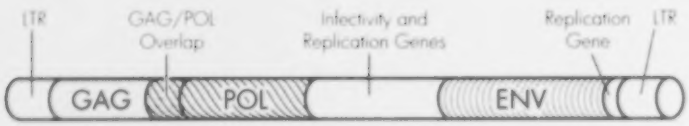
The **POL** gene provides the code for three enzymes: reverse transcriptase, protease, and integrase. Reverse transcriptase helps transcribe RNA into DNA. Protease cleaves viral polypeptide chains into usable proteins. Integrase facilitates the insertion of viral DNA into the host DNA.

In addition to GAG, ENV, and POL, the genome contains six other genes. These smaller genes code for proteins that regulate HIV replication.



Both ends of the HIV genome are "capped" with a similar sequence of nucleotides called **long terminal repeats (LTRs)**. The LTRs contain sequences that enhance the replication of new viruses.

A Model of the HIV Genome



Materials

clay (5 colors: include brown, yellow, green, blue, and red)
metric ruler

Steps

1. The table below illustrates the approximate gene lengths in a desktop model of the HIV genome.
2. Roll lumps of clay into pencil-thick cylinders.
3. Use a knife to cut each clay roll to the length indicated below.
4. Assemble the sections end-to-end.

brown clay	1.6 cm	LTR
yellow clay	3.8 cm	GAG
green clay	.8 cm	GAG/POL overlap
blue clay	6.4 cm	POL
red clay	3.2 cm	several genes that enhance replication and infectivity
blue clay	6.4 cm	ENV
red clay	.6 cm	partial gene that enhances replication
brown clay	1.6 cm	LTR

Questions

1. How many LTRs belong to the HIV genome? Where are they located?

2. Identify the products of the GAG, POL, and ENV genes.

3. If each centimeter of model length represents 400 bases, about how many bases compose a complete genome of HIV?

Part B: HIV Types, Groups, Subtypes, and Strains

HIV has a high rate of mutation. During a cycle of replication, the infected host cell will manufacture thousands of new viruses. Mistakes made during copying of the virus genome will produce variants of the virus. Thus, a person infected with a single virus will soon harbor an array of closely-related HIV variants. Some variants may differ in their host cell preference. Others may replicate at a slower rate. Some may become more resistant to the anti-HIV drugs, and still others may become more resistant to the host's immune system.

Much of HIV's genetic diversity can be tracked to the error-prone action of reverse transcriptase. When this enzyme copies viral RNA into DNA, mutations are common, with at least one mutation during each replication.

With this high degree of mutation one would expect HIV to rapidly evolve. In fact, through close analysis of genomes from HIV derived from many places around the world, scientists have been able to classify HIV isolates into many groups. There are two major **types** of HIV recognized worldwide. The differences between these two types are significant enough to distinguish them as separate viruses. HIV type 1, or HIV-1, is predominant in the United States and worldwide. HIV type 2, or HIV-2, is found primarily in Western Africa.

Through close analysis of the genomes of HIV-1 isolates, researchers further subclassify HIV-1 into two widely divergent **groups**, group M (major) and group O (outlier). Group O viruses (found mainly in Africa) are so different that they can be missed by some of the standard tests used for HIV screening. The group M viruses can be further classified into about 10 **subtypes**, identified by letters of the alphabet (subtype A, subtype B, subtype C, etc.) While different subtypes can readily be identified on the basis of their genetic structure, scientists have thus far been unable to identify any subtype-specific characteristics with certainty. The rapid spread of specific subtypes in certain regions of the world (e.g., subtype E in Southeast Asia and subtype C in India and southern Africa) has led some scientists to speculate that these variants may have enhanced transmission capabilities.

The study of genetic subtypes and their distribution has been helpful in tracking the spread of the HIV epidemic. While subtype B variants have long been the only subtype identified in the United States, isolated cases of non-subtype B infections are beginning to appear as a result of global travel.

Finally, every virus isolate (HIV sample taken from a person) studied to date has been shown to have a unique genetic structure (no isolates are exactly alike), so each particular isolate is called a **strain**.

Scientists study the sequence of nucleotides in HIV genes to identify different types, groups, sub-types, and strains. Examine the six nucleotide sequences below. Suppose all six sequences were taken from the same region of different HIV proviruses. Analyze the sequences to group them according to similarities and differences. A good way to start is to divide the sequences into groups of three to represent the code for an amino acid (TTT, AAA, etc.). Hint: Sequences a, c, and e are similar, but what differences do they have?

a. T-T-T-A-A-A-C-G-C-G-C-A-T-T-T-A-A-G-C-C-C-G-C-A

b. A-T-G-G-G-C-A-T-C-T-T-A-A-C-G-C-G-C-G-A-T-T-A-T

c. T-T-T-A-T-A-G-C-G-G-C-A-A-A-A-A-A-G-C-C-C-G-C-A

d. A-T-G-C-C-G-A-T-C-T-T-A-A-C-G-C-G-C-G-A-T-T-A-T

e. T-T-T-A-A-A-G-C-G-G-C-A-T-T-T-A-A-G-C-C-C-G-C-A

f. A-T-G-T-C-C-A-T-C-T-T-T-T-C-G-C-G-T-C-G-T-T-A-T

1. Place the above sequences into two groups that represent a large difference between sequences. These could represent the division between HIV-1 and HIV-2. What is your grouping scheme based upon?
2. Look at the group of sequences that you labeled HIV-1. Identify two groups of sequences that best represent different subtypes of that larger group. Repeat this exercise for HIV-2. What is your grouping scheme based upon?
3. Finally, identify two groups of sequences that best represent different strains of the same virus subtype. That is, identify the most similar pairs of sequences. What is your grouping scheme based upon?

The Genetics of HIV

Objective

Students will model the HIV genome to understand the sequence of genes and their products. Students will explore how HIV's replication process produces many variants. HIV's high mutation rate is an important concept because it is one major reason why treatments for AIDS are difficult to develop.

Teacher Notes

Part A: The HIV Genome

Refer back to the comparison of viral and human genomes on page 16. Explain to students that parts of the HIV genome (genes) provide the code for structural and functional parts of the virus.

Part B: HIV Types, Groups, Subtypes, and Strains

Explaining genetic variants: remind students of the game of "telephone." If appropriate, you may want to play a quick round of the game. Organize the class into rows of players. Present a sentence of 10 words to the first player in each row. That person must then whisper the sentence to the next player so that no one else can hear. The last player in each row records the final version of the sentence. Compare and contrast the first and final arrangements. Explain how this variation in the code as it was "replicated" between players is similar to the appearance of genetic variants.

THE NINE GENES OF HIV

In addition to POL, ENV, and GAG, the HIV genome contains six more genes that regulate the replication and infectivity of HIV.

rev - enhances production of structural mRNA
tat - increases the level of viral mRNA production
nef - lowers the level of viral mRNA production
vif - (virion infectivity factor) makes the virus infective
vpr - essential to replication, but function unclear
vpu - essential to replication and release from the host cell

The tat and rev genes code for proteins essential for HIV replication. The vif, vpr, and vpu genes code for proteins that enhance the replication rate and infectivity of HIV. The tat, rev, and nef genes are regulatory genes.

HIV TYPES, GROUPS, SUBTYPES, AND STRAINS

Type (HIV-1, HIV-2)
  Group (groups M and O of HIV-1)
    Subtype (further subclassifications of HIV-1 and HIV-2)
      Strain (any particular virus isolate (variant))

Answers to Student Questions

Part A

1. Two; located at the ends of the genome
2. GAG - structural proteins; POL - enzymes; ENV - envelope proteins
3. About 10,000 (the model is too imprecise for an exact number)

Part B

1. Virus I: a, c & e. Virus II: b, d & f. The scheme is based upon the most substantial differences which divide the six variants into two types.
2. Virus I: one subtype is represented by a & e; another subtype is represented by c. Virus II: one subtype is represented by b & d; another subtype is represented by f. The grouping is based upon increasing similarity in nucleotide sequence.
3. The grouping is based upon the most similar nucleotide sequence.
   Sequences a & e could be strains of the same subtype.
   Sequences b & d could be strains of another subtype.

Vocabulary

ENV - HIV gene that codes for the viral envelope proteins

GAG - HIV gene that codes for the capsomeres of the capsid and matrix protein

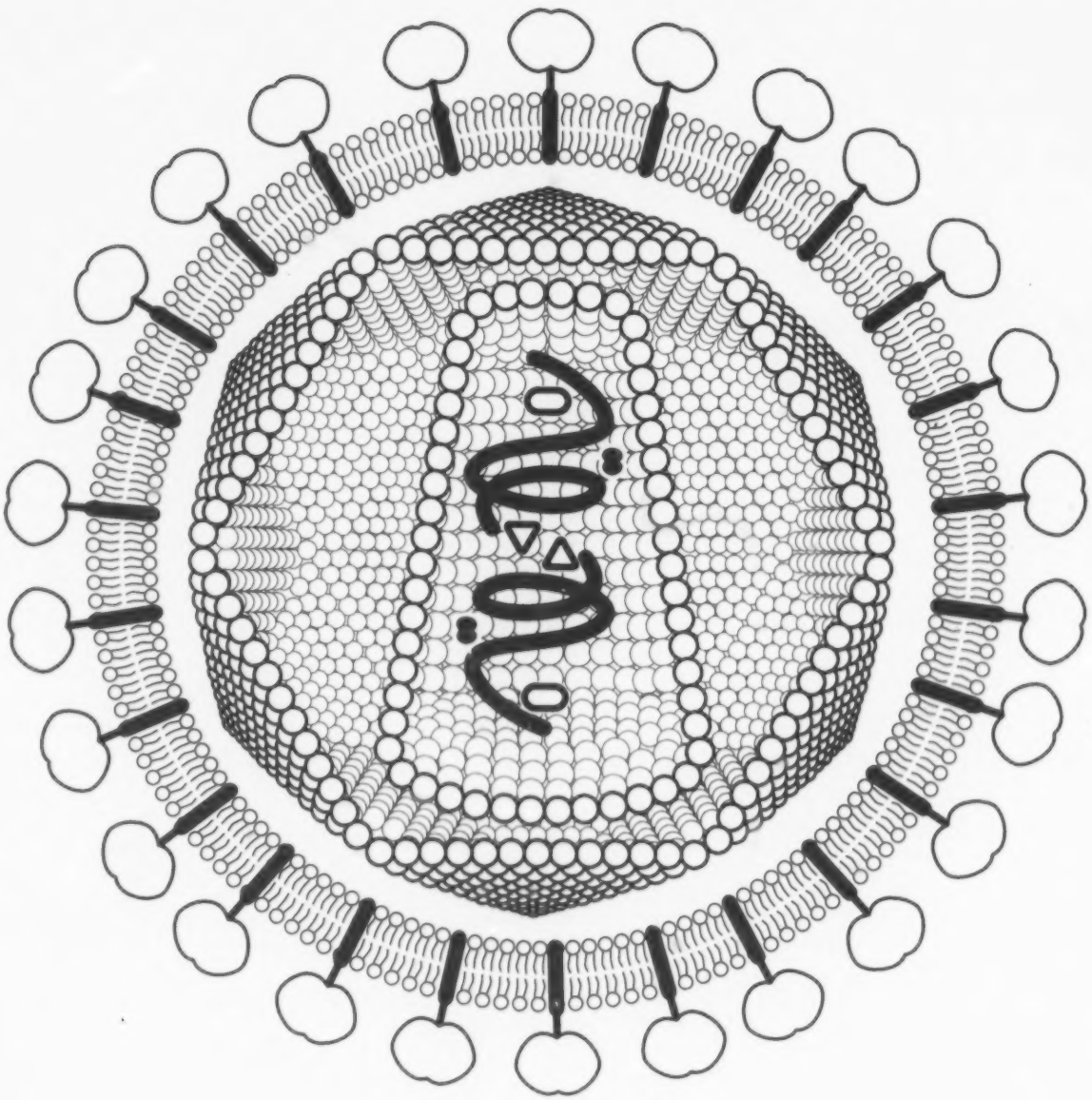
genome - the complete set of an organism's genes

HIV-1 (Human Immunodeficiency Virus-1) - HIV type that is the predominant type in the United States and worldwide

HIV-2 (Human Immunodeficiency Virus-2) - HIV type that is relatively rare in the United States, but more common in West Africa

LTR (long terminal repeats) - repeating nucleotide sequence found at either end of the provirus DNA

POL - HIV gene that codes for the three viral enzymes



TEACHER SUMMARY

CHAPTER THREE

The Immune System

Defending the Healthy Cell

Curriculum Connections

- The Nature of Disease
- Human Immune Response
- Blood Type
- Red and White Blood Cells

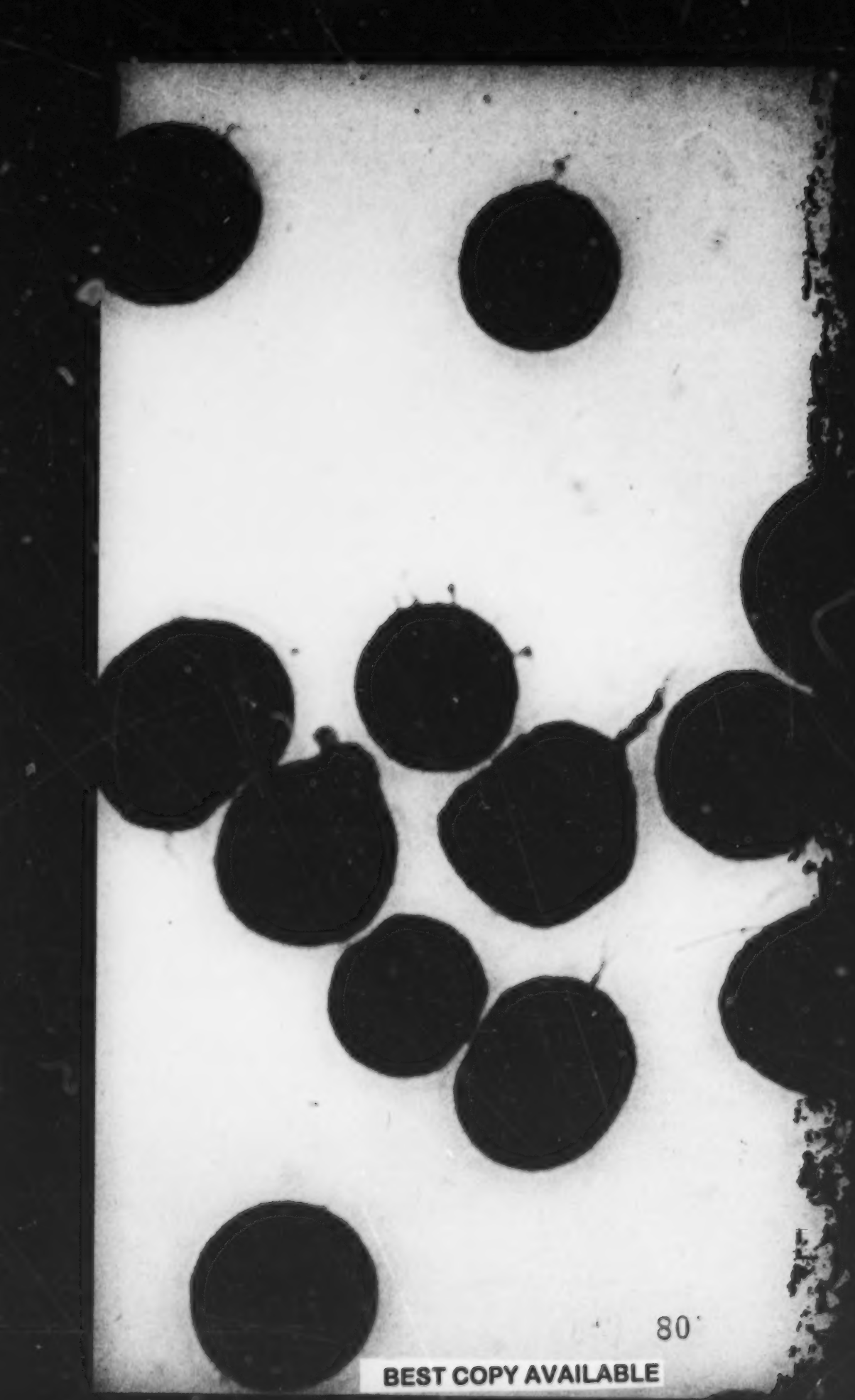
Chapter Concepts

Chapter Three introduces the human immune response system, consisting of both physical barriers (e.g., skin, saliva) and the specific reactions of white blood cells to foreign matter. The white blood cells perform many roles from phagocytosis (ingesting foreign cells) to directing the immune response through intercellular communication.

The Helper T Lymphocyte, or T_H cell, is the coordinator of the immune response cells. HIV primarily infects the T_H cell. Once the HIV infection kills sufficient numbers of T_H cells, the HIV-infected person dies of various microbe infections. The death of one kind of cell in the human body (in sufficient numbers) can stop the proper functioning of the human body.

National Science Education Standards

Content Standards 9–12
Content Standard B: Chemical Reactions
Content Standard C: The Cell; The Behavior of Organisms
Content Standard G: History and Nature of Science; Historical Perspectives (Molecular Biology)



The Immune System

Defending the Healthy Cell

A Hands-On Investigation

Lab Activity
Antigen/Antibody Response

The Immune Response

Primary and Secondary Immune Response

HIV Infection and T Cell Counts

BEST COPY AVAILABLE

A Hostile Environment

Imagine a planet overrun with deadly microbes. There is no escape. Lethal germs infest the air, water, and food.

This is our world. From birth to death, we are never alone. We are surrounded (and covered) with potentially deadly microbes. These disease-causing agents, however, are kept in constant check by our body's defenses.

Our first line of defense is intact skin. Skin is a living coat of armor that forms a physical barrier against infection. Places that lack regular skin have other ways of countering microbe invasion. Tears contain germ-killing substances that guard the fragile membranes of the eye. Like tears, saliva contains an enzyme that kills some foreign microbes. Germs that make it past the saliva-coated mouth are swallowed. Along with undigested food, they are transported to the stomach. There, most microbes are destroyed by powerful digestive acids.

Your respiratory system uses a lining of mucus to keep out foreign particles. This sticky stuff works like fly paper, trapping airborne particles. Tiny hairs that coat the respiratory passages push the mucus upwards to the mouth. Swallowing sends the mass to the acid-filled stomach.

Even with all these defenses, some germs gain entry to our bodies through breaks in the skin and penetration of delicate mucous membranes. The fight, however, is just beginning. A second line of defense is formed by special cells that circulate within your body. Working together, these white blood cells form the **immune response**.

Immune cells originate from and move around through the **lymphatic system.** Lymph is a fluid confined to the lymphatic vessels. In addition to maintaining the proper fluid concentrations in tissue spaces, the lymphatic system aids in the development of immune cells and disperses immune cells throughout the body.

In order to destroy intruder organisms, the white blood cells first need to know which cells and microbes belong and which do not. Cells that comprise the body are identified as "self." Cells (or particles) that are foreign are considered "non-self." The recognition of self versus non-self is based upon tiny markers that cover cell surfaces. These molecules act like I.D. cards. In chemical language, they identify a cell as "self" or "non-self."

When a defense cell encounters another cell, it examines the membrane surface. If the search uncovers a proper I.D., the defense cell moves on. If, however, the cell does not have a "self" marker, things happen. A signal mobilizes an immune response. Specialized cells (called T cells and B cells) identify and destroy the the non-self invaders. Even when the danger has passed, some immune cells retain a chemical memory of the attack, ensuring a swifter and more effective response to the invader's next appearance.

Questions

1. Identify and describe the body defense that would be most active in the following situations.
   a. You inhale a microbe that can produce tuberculosis.

   b. A staph bacterium makes contact with your exposed skin.

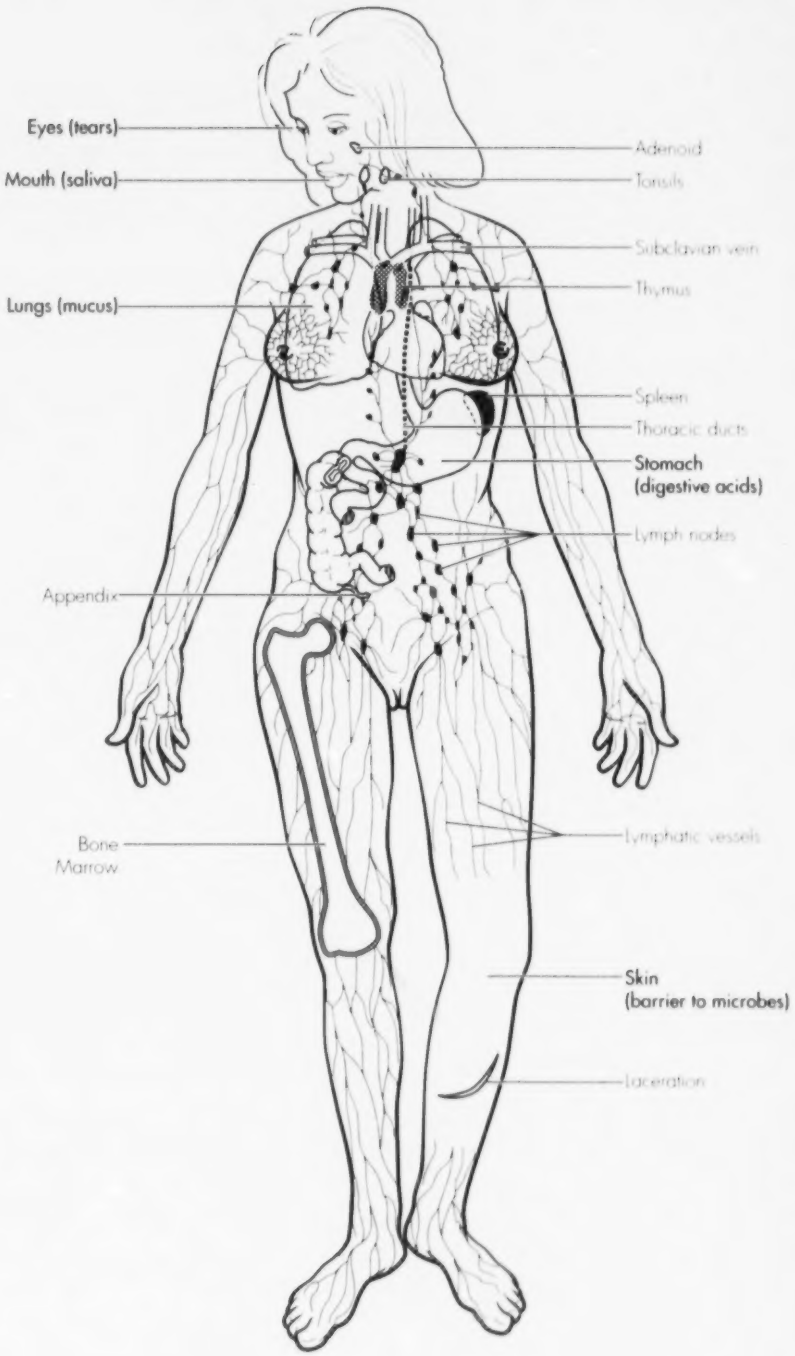
   c. A mosquito injects a parasite into your blood.

   d. You eat a sandwich in which the meat has spoiled.

   e. A speck of dust covered with bacteria gets in your eye.

2. Compare and contrast the passive defense mechanism of skin with the more active response of immune cells.

3. Some medications cannot be given orally. Instead, they must be injected directly into the muscles or bloodstream. Explain.



A Hostile Environment

Objective

Students will use a diagram of the human body to explore how the human body defends itself against infection, from intact skin to highly specific responses by white blood cells.

Teacher Notes

Discuss the prevalence of microbes within the environment. Explain that for people with a healthy immune response, most microbes that one encounters on a daily basis are harmless. When this response is suppressed, however, harmless microbes may become deadly.

Have students identify the different body defenses against infection. Explain how each defense protects us from external microbes. The coverage should include:

a. intact skin
b. stomach acid
c. mucus lining of the respiratory tract
d. enzymes in tears and saliva
e. white blood cells.

Explain that people who receive transplanted tissues or organs often are administered "immunosupressant drugs" to reduce rejection by the body. Challenge students to uncover the reasons for the administration of these drugs (reduced rejection of non-self tissues).

The Lymphatic System

Before discussing the lymphatic system, you may wish to begin by surveying the class for students who have had a tonsillectomy. If appropriate, have the students describe the symptoms leading up to the operation, the tonsillectomy, and the recovery period. Use this experience to assess the depth of prior knowledge of the lymphatic system.

The lymphatic structures identified on the student sheet are described in the margin boxes. For a more complete description of the cells involved in the immune response, see pages 75–81.

LYMPHATIC STRUCTURES

Tonsils
The tonsils consist of several nodules of lymph tissue that form a strategically placed ring near the oral cavity.

Lymph Nodes
Have students locate the lymph nodes at the back of their neck. They can find them by pressing gently at "collar-height." Explain that these (and other nodes) often swell when we become sick. Their swelling is associated with the increased populations of white blood cells. Pathogens transported in the lymph are destroyed by the nodes' concentrated population of immune cells.

Thymus Gland
The thymus gland is located in the center of the upper chest. In infants, this gland helps produce a kind of white blood cell (T lymphocytes) and chemicals that fight off infection. It is also the site of development for mature T lymphocytes.

Answers to Student Questions

1. a. Mucus lining of respiratory tract
   b. Physical barrier of intact skin
   c. Response of circulating immune cells
   d. Digestive action of saliva and stomach environment
   e. Digestive enzymes in tears
2. The skin is a physical barrier that keeps invaders out of the body. It does not actively seek, detect, or restrict foreign particles. The immune cell response is based upon the recognition of specific particles that have gained entrance into the body. This response targets and destroys invaders.
3. The drugs might be broken down by the digestive chemicals.

Vocabulary

immune response - a cellular defense mechanism using a variety of specific cells and proteins to destroy foreign materials such as microbes

LYMPHATIC STRUCTURES

Thoracic Ducts
These large lymph vessels return lymph into the major veins of the blood circulatory system.

Lymphatic Vessels
A network of lymph-containing vessels drain fluid from intercellular spaces and provide a route for lymphocyte distribution.

Appendix
Like other satellite organs of the lymphatic system, the appendix maintains a large population of immune cells.

Bone Marrow
T and B lymphocytes (two kinds of white blood cells) originate here. B lymphocytes also mature here. White blood cells that will develop into T lymphocytes migrate to the thymus.

Spleen
The spleen is the largest lymphatic structure in the body. Unlike lymph nodes, the spleen does not filter lymph. It is, however, the site of B lymphocyte production. Phagocytes (white blood cells that eat foreign particles) within the spleen remove pathogens and worn-out blood cells.

Adenoid
Also considered a tonsil, the adenoid is a single lymph nodule located at the back of the nasopharynx.

Subclavian Vein
This blood vessel returns lymph to the blood circulatory system.

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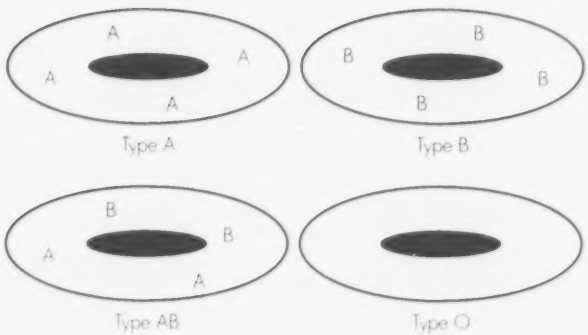
Lab Activity

Antigen/Antibody Response

Blood Types

Red blood cells, like other body cells, have proteins with carbohydrate chains attached that stick out from the cell membrane. Some of these protein-carbohydrate complexes are called **antigens**. Antigens are substances, proteins, particles, or whole microbes that are recognized by the body as foreign (non-self). Your body produces specialized proteins, called **antibodies,** that recognize, attach to, and fight antigens. Antibodies are highly specific and circulate within the blood plasma. For example, people who are infected with HIV produce antibodies to the virus.

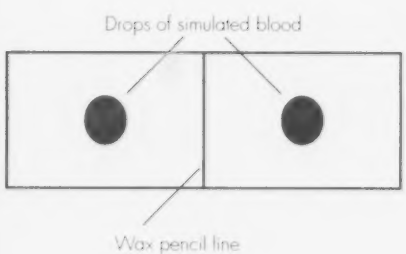


Red blood cell membranes have proteins and carbohydrates in them known as the O-A-B system. This system is used to distinguish four major blood groups: A, B, AB, and O. Differences in blood type are due to the presence or absence of A or B antigens on the membranes of red blood cells. A and B are types of antigens that may be found in a person's blood. Type O means that there are no antigens present on the red blood cells. It is not known why red blood cells have antigens on them, but your blood only contains antibodies for antigens in other blood types, not your own type.

In this activity, you will simulate blood typing. Two reagent chemicals will be added to simulated blood samples of unknown type. The pattern of serum "clumping" will be analyzed to identify each blood type.

Materials

mixing sticks
clean dry slide
wax pencil
simulated blood serum
anti-A sera
anti-B sera



Steps

1. Use a wax marking pencil to draw a line down the middle of a clean, dry slide. Place one drop of simulated type A blood on each side of the slide.
2. Add a drop of anti-A serum to one of the blood drops. With an unused mixing stick, stir the mixture.
3. Add a drop of anti-B serum to the other drop. With an unused mixing stick, stir the mixture.
4. Wait several minutes. Record your observations.
5. Using clean slides and mixing sticks, repeat steps 2–4 using drops of simulated sera representing type B blood, type AB blood, and type O blood.
6. Use this technique to uncover the identity of the unknown simulated blood samples supplied by your instructor.

Questions

1. Why was it important to use simulated blood?

2. Describe how anti-sera are used to identify blood groups.

3. Identify the blood type(s) of your unknown, simulated blood samples.

4. Suppose there were three separate surface proteins (A, B, C). How many different blood groups could be formed?

5. What is happening when blood "clumps"?

6. What happens when a person is given a transfusion of the wrong blood type?

BLOOD GROUPS

There are at least 30 different antigens that are identified with red blood cells. Most of these antigens are found on the cell membrane but do not cause transfusion reactions. A transfusion reaction produces clumping of blood cells that can lead to death. Two groups of antigens are responsible for this severe and life-threatening reaction. They are the O-A-B system and the Rh system.

Because each of us inherits one (O or A or B) gene from each parent (and O can be considered neutral), there are four major blood types based on the O-A-B system:

Type	Genotypes	Percent (US population)	Antigens	Plasma Antibodies
O	OO	47		Anti-A and Anti-B
A	AO, AA	41	A	Anti-B
B	BO, BB	9	B	Anti-A
AB	AB	3	A and B	

The Rh typing is slightly more complex. There are six distinct antigens which are known as Rh factors (C, D, E, c, d, e). Only the D factor, whose transfusion reaction is most severe, is considered when typing individuals as Rh positive or Rh negative.

Lab Activity

Antigen/Antibody Response

Objective

Students will use blood typing kits to depict the antigen/antibody reaction.

Teacher Notes

Explain that antigens are substances that are recognized by the body as foreign (non-self). The body produces antibodies that recognize and bind to antigens. Antibodies are highly specific and circulate within the blood plasma. Antibodies that bind to disease-causing agents can attach in a manner that deactivates or destroys the microbe. In addition, the resulting antigen-antibody complex can activate, attract, and heighten the response of phagocytes. Later sections of this chapter will discuss plasma cells, the cells which produce antibodies. Antibodies to HIV appear in HIV-infected people.

Materials

Blood typing activities must not involve classroom blood letting. Instead, simulated blood should be used in its place. The precipitation reaction of the simulated blood mimics the agglutination of real blood samples. Simulated blood and blood typing kits are available from large scientific supply companies.

Laboratory Precautions

It is good laboratory practice for students to treat all blood samples (even simulated sera) as if they contained infectious agents. Students should not touch any samples directly. All mixing sticks should be disposed of according to the instructions supplied with the testing kit. Surfaces should be cleansed appropriately.

Answers to Student Questions

1. To prevent the transmission of pathogens (including HIV) that might be carried in untreated blood
2. The antigen/antibody reactions form a clumping of the blood cells. The clumping indicates that a specific antigen was present. The presence of these antigens are then used to type the blood.
3. Answers will vary
4. Eight
5. Antibodies bind to their complementary antigen sites on the surface of the red blood cell.
6. Foreign blood is identified as "non-self." Antibodies produced in the body of the transfusion recipient bind to the foreign cells. The binding produces clumps that may block critical blood vessels, and cause severe damage, if not death.

Vocabulary

antigens - foreign substances that stimulate the production of antibodies in the blood

antibody - protein in the plasma produced by plasma cells in reaction to antigens which can attach in a manner that deactivates or destroys the microbe

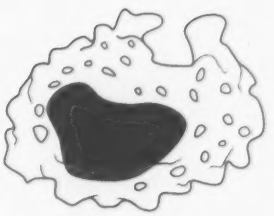
The Immune Response

Part A: Immune Cells

Suppose that intruders have made it past the first line of body defenses. Now, it is up to the **white blood cells** (WBCs) of the immune system to rid the body of these infectious agents. Like the military defenders of a nation, the WBCs are specialized for specific missions.

Macrophages

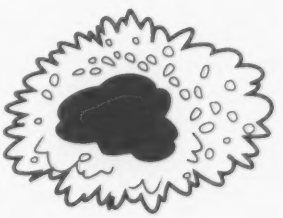
When a macrophage recognizes a foreign invader, the macrophage surrounds and engulfs the intruder in a process called **phagocytosis.** Within the macrophage, the ingested particle is partially broken down. Intact parts of the particle (antigens) are displayed on the surface of its macrophage. These displayed parts tell other cells that an intruder is present.



Macrophage

Natural Killer Cells

Natural killer cells are general patrol cells. They look for cells that do not carry surface proteins marked "self." NK cells kill foreign cells, cells infected by a virus, or cancerous cells. The NK cell uses special proteins to kill these "non-self" cells.

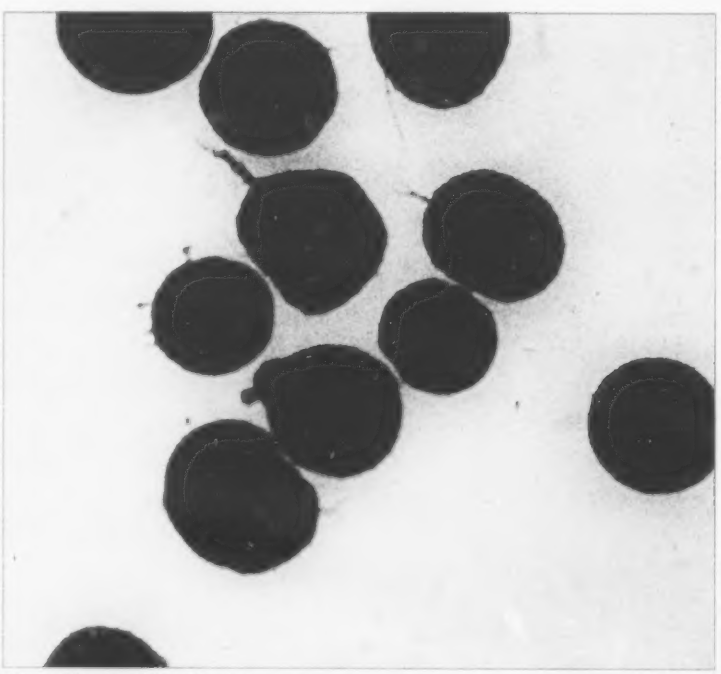


Natural Killer cell

Lymphocytes (B Cells and T Cells)

Have you seen wanted posters in the supermarket or post office? This is how police tell everyone about people who may be dangerous. At a somewhat different level, antibodies circulate in your blood, putting "wanted posters" on foreign matter. Antibodies target and bring attention to specific intruders. Antibodies pull other immune cells into the attack which destroy all of the particles that fit the wanted-poster profile.

The immune cells that target and destroy specific intruders comprise two groups of white blood cells: **B lymphocytes** and **T lymphocytes**. These cells are named after the site in which they mature. B cells mature in the bone marrow. T cells mature in the thymus gland.



COURTESY OF NIAID, NIH

Normal human T lymphocytes

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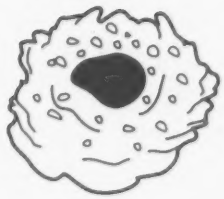
TYPES OF B CELLS

Plasma cells
When activated, some B cells develop into plasma cells which produce antibodies. Antibodies released by these cells bind to the antigens found on the invader's surface. A coat of antibodies can disable, destroy, and bring attention to the intruder.

Plasma cell

Memory B cells
Some B cells become modified into memory cells. These memory cells maintain a record of the specific antibody production. If the antibody is needed again, the memory cell will have the same antibody manufactured more quickly than during the first encounter.

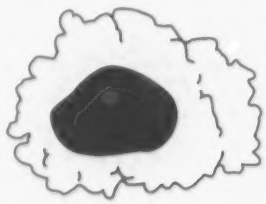
Memory B cell



TYPES OF T CELLS

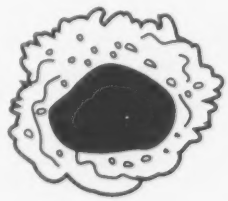
Helper T cells (T_H cells)
These cells take on the role of a general by regulating the activities of almost all other immune cells. They direct the war against infection by releasing a variety of signaling molecules called **lymphokines**. T_H cells are sometimes called "CD4" or "T4 cells" because the membrane contains CD4 proteins.

Helper T cell



Memory T cells
Like memory B cells, these cells remember what happened and are ready to respond quickly to an antigen when it returns to the body. T_H cells stimulate the production of these cells.

Memory T cell

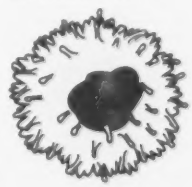


Cytotoxic T cell

Cytotoxic T cells (Killer T cells)
These cells can chemically "scan" a cell for virus infection. Cells that have been infected are destroyed by this killer T cell.

Suppressor T cells
These cells call off the war after the infection has ended.

Suppressor T cell



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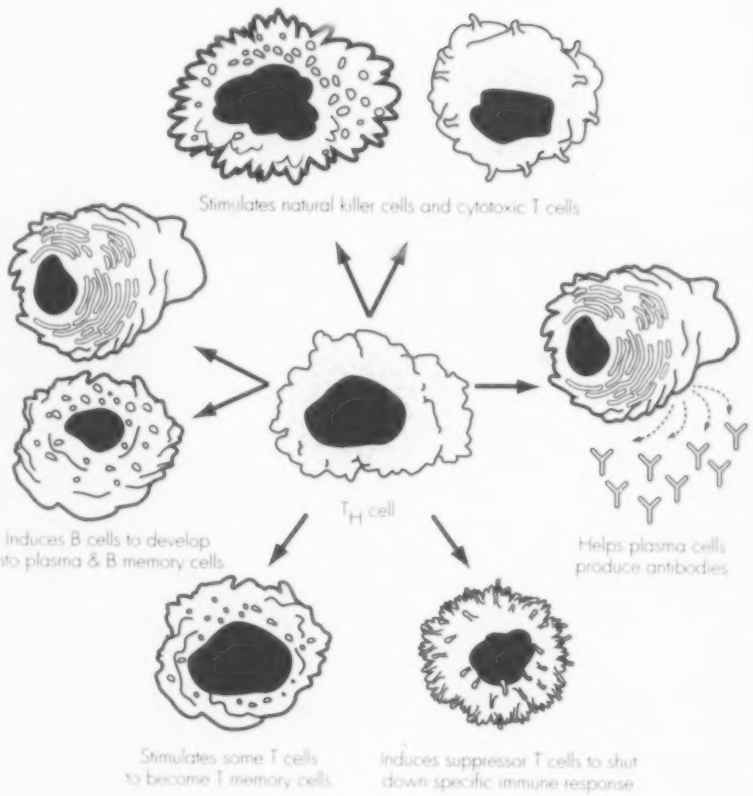
Coordination of the Immune Response: T_H Cell

Every army needs a general. In the immune response, that job is entrusted to the T_H cell. Before the T_H cell can take command, however, it must be "switched on." T_H activation results from very specific contact with a macrophage.

In order to activate a T_H cell, a macrophage must first engulf a foreign particle. After the ingested particle is partially broken down, antigens are displayed on the surface of the macrophage. T_H cells bear receptor sites for both a specific displayed antigen (non-self) and the macrophage's normal protein markers (self). If the T_H cell with the matching receptor combination contacts the antigen-displaying macrophage, binding occurs. This reaction "turns on" the T_H cell.

The activated T_H cell produces and releases its own variety of lymphokines (signaling molecules) which activate, induce, and heighten the immune response. The effects of these molecules are shown in the diagram to the right.


Stimulates natural killer cells and cytotoxic T cells
T_H cell
Induces B cells to develop into plasma & B memory cells
Helps plasma cells produce antibodies
Stimulates some T cells to become T memory cells
Induces suppressor T cells to shut down specific immune response

T_H cell coordinates the immune cell response

Questions

Suppose a huge portion of the body's T_H cells were killed by a virus. How might this change the immune response? Identify one role of the T_H cell on each line below. Next to each role, describe the specific consequences that would occur if the role were not performed.

1. _____

2. _____

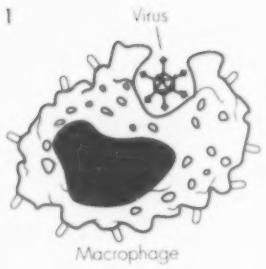
3. _____

4. _____

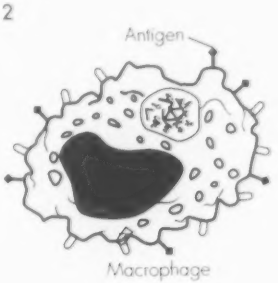
5. _____

Part B: General Example of Immune Cell Interaction

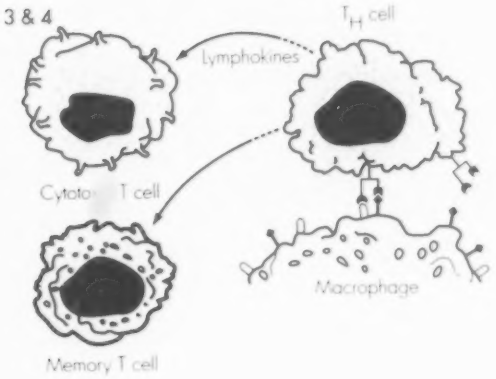
The immune cells interact in many ways to produce a complete immune response. This is only one example.



1. A macrophage engulfs the virus. The virus is ingested.

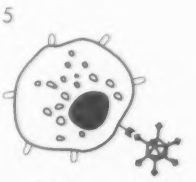


2. Antigens (derived from the destroyed virus) are displayed on the macrophage membrane. Like membrane proteins, these fragments can be identified through physical contact.

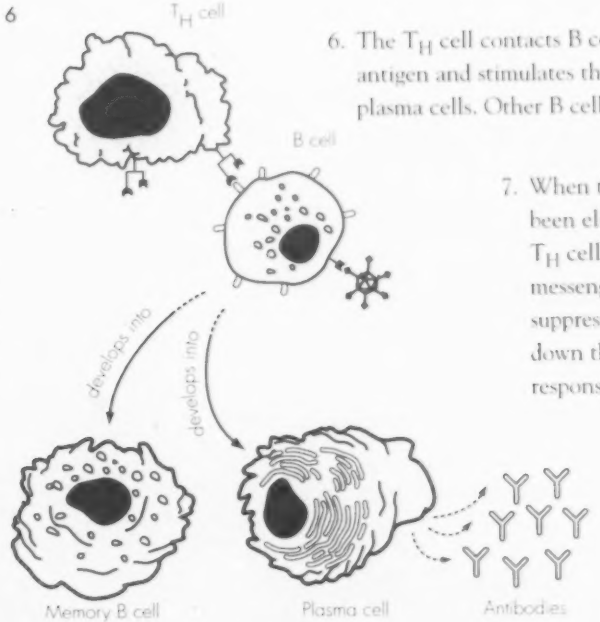


3. A T_H cell, bearing receptors for both the virus fragments and the macrophage membrane proteins, binds to the macrophage surface. As the cells bind, the macrophage activates the T_H cell.

4. The activated T_H cell releases lymphokines that stimulate the production of cytotoxic T cells and memory T cells.

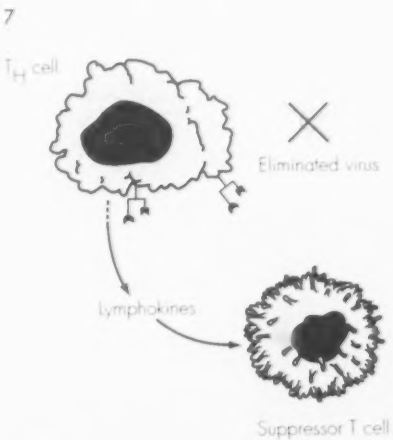


5. B cells bind with the specific viral antigen.



6. The T_H cell contacts B cells capable of binding to the same antigen and stimulates them to develop into antibody-releasing plasma cells. Other B cells become memory cells.

7. When the virus has been eliminated, the T_H cell releases protein messengers that instruct suppressor cells to shut down this specific immune response.



The Immune Response

Objective

Students will look at representations of different types of white blood cells to understand the immune response. The focus is on the role of lymphocytes, particularly T cells, in fighting infection. T_H cell activation and its interaction with other white blood cells is important because this cell is the target of HIV. When this coordinating cell is killed by HIV, the entire immune response suffers.

Teacher Notes

Part A: The Immune Cells

Many students have the misconception that the immune response of white blood cells is limited to non-specific ingestion and destruction of foreign particles. Point out that the complete response is a very complex process that involves many types of white blood cells, each with a specific role. This book does not discuss certain other types of white blood cells (i.e., megakaryocytes, basophils, mast cells, eosinophils, and neutrophils) because they do not play a primary role in the immune response to HIV. However, they are important to give a complete view of the immune response. Most biology textbooks discuss the functions of these cells. Students may be interested in extra credit study on these cells.

Macrophages are a kind of phagocyte that have the additional ability to display antigens on their membranes to be "read" by lymphocytes.

Have students identify specific white blood cells associated with each role listed below:

non-specific attack (target any foreign particle) — macrophage
specific attack (target specific antigen) — lymphocytes
manufacture and release antibodies — plasma cells
release toxic chemicals that kill large pathogens — natural killer cells
sound the alarm — macrophages (also antibodies)
attract phagocytes to antigens — antibodies produced by plasma cells
maintain an attack memory — memory T and B lymphocytes
activate the immune response — macrophages, T_H cells
suppress the immune response — suppressor T lymphocytes

T_H CELLS AND CD4 RECEPTORS

HIV enters a cell by binding its gp120 glycoprotein with a CD4 receptor on a cell's membrane. T_H cells have more CD4 receptors than other cells and are therefore the main cell that HIV infects. (Memory T cells, some macrophages, and some brain cells also have CD4 receptors.) In current scientific literature, T_H cells (and memory T cells) are often, if not exclusively, called T4 cells or CD4 cells to designate them as cells that are affected by HIV infection. This book uses the term T_H to make it clear to students what this cell does (i.e., "help" the other cells to respond). Since T_H cells stimulate the formation of memory T cells, a depletion of T_H cells leads to a depletion of memory T cells.

CO-FACTORS IN HIV INFECTION

Scientists have identified co-receptor sites on T_H cell membranes. These receptors have been named, "fusin." CD4 alone is not sufficient to allow HIV to fuse with target cells and infect them. In people who are infected with HIV, fusin becomes an essential gateway to cell infection. The normal role of fusin is not known yet, but evidence shows that fusin binds to signaling proteins called chemokines.

A small number of individuals do not become infected with HIV despite numerous exposures. Others who are already infected do not show a decline in immune function over many years. Scientists are exploring the relationship between these unique individual cases and the fusin/chemokine findings. One theory is that the circulating chemokines may compete with HIV for the available co-receptor sites. When enough natural chemokines are present, they may lock out HIV and prevent its entrance into target cells.

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Lymphocytes (B cells and T cells)

Draw a cartoon wanted poster on the chalkboard. Write the terms "specific attack" and "non-specific attack" at the side of the poster. Have students discuss the nature of each defense process.

Review the activation of a T_H cell by a macrophage. Discuss the significance of the macrophage's antigen-presenting behavior. T_H cells are activated also by cells other than macrophages. For the purposes of this book, however, this general description is adequate. Stress the importance of the T_H cell in the immune response. Explain that HIV targets the T_H cell specifically. Eventually, the HIV-infected cell dies. Have students discuss how this would affect the immune response as a whole.

Part B: General Example of Immune Cell Interaction

Review macrophages, B cells, and T cells. Copy page 93 onto a transparency sheet or distribute copies to the class. Explain that this diagram represents the critical interaction between several cells involved in the immune response.

Model Building: Supply students with several different colors of modeling clay. Challenge each student to create clay models illustrating immune cell interactions.

Immune Cell Skit: Students may be interested in performing a short skit about the immune response. Each student can play one kind of white blood cell.

TAXONOMIC KEY

A taxonomic key is a tool that is used to identify objects, organisms, and cells. A key is composed of a series of paired statements. To use the key, start at the first statement pair. Select the one statement that best describes your object. That statement may include either the identity of the object or a "go to" number. Follow the number to your next statement pair. Continue along this journey until you determine the unknown object. Here's a simplified key for O-A-B blood types.

1. a. Red blood cell has no O-A-B surface antigens . . . . . type O blood
   b. Red blood cell has surface O-A-B antigens 2
2. a. Cell has both A and B antigens . . . . type AB blood
   b. Cell has either (but not both) A and B antigens . . . 3
3. a. Cell has only A antigens . . . . . type A blood
   b. Cell has only B antigens . . . . . type B blood

Challenge students to develop their own taxonomic keys to assess their subject mastery.

Assessment

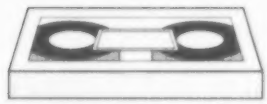
Students may develop a taxonomic key that can be used to distinguish groups of white blood cells or the kinds of lymphocytes. Divisions can be based upon characteristics such as specificity of response, type of response, and type of target. Keys could begin with statement pairs like the two below:

1. WBCs that are not involved in immune response . . . . . megakaryocytes
   WBCs that are involved in immune response 2

or

1. a. Lymphocytes that mature in the bone marrow . . 2
   b. Lymphocytes that mature in the thymus gland . . 3

Answers to Student Questions



Video Connection:
See immune response animation. (5:46)

Part A

T_H cell functions and consequences that would occur if the role were not performed.

1. Stimulates cytotoxic T cells; viruses hidden within infected cells would not be detected.
2. Induces B cells to change into plasma cells; without sufficient plasma cells, antibody production might not be effective.
3. Helps plasma cells produce antibodies; there might not be sufficient antibodies to fight off infection.
4. Stimulates production of memory B and memory T cells; the reappearance of the antigen would not stimulate an enhanced memory response.
5. Induces suppresser cells to shut down response; energy and materials would be wasted on maintaining a nonessential defense.

Vocabulary

B lymphocyte (B cell) - cell that develops into antibody-secreting plasma cell or memory cell

lymphocyte - white blood cell that responds to a specific antigen

lymphokines - chemicals released by the T_H cells that regulate the response of other immune cells

phagocytosis - process of engulfing, ingestion, and digestion of foreign particles

T lymphocyte (T cell) - cell with several roles including regulation of the immune response

white blood cell - blood cells that do not contain respiratory pigment, but instead participate in the maintenance of an organism's healthful state

Primary and Secondary Immune Response

Part A: Memory Response

Law enforcement agents use a book of "mug shots" to help identify previous lawbreakers. The mug shots comprise a photo library of individuals who were arrested for criminal acts. Like these agents, some cells of your immune system also maintain a record of previous intruders. This recall is the basis of the memory response.

The first appearance of an infectious agent stimulates the **primary immune response**. During this response, the intruder is identified and eliminated. As part of this process, T_H cells activate antigen-specific T and B memory cells. A memory cell is dedicated to recalling only one type of antigen. Since your body encounters thousands of antigens, its mug shot portfolio must contain an equal number of different memory cell types.

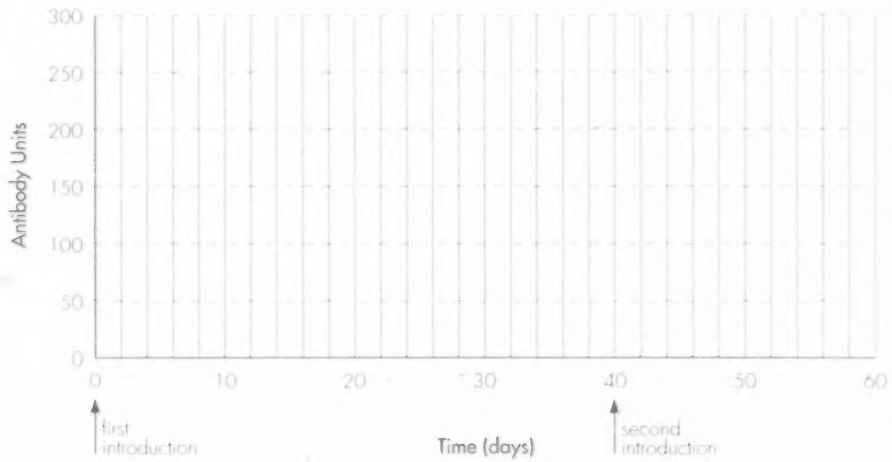
If an antigen reappears, the specific memory cells act quickly. Memory T cells become active T cells. They produce a **secondary immune response**. Plasma cells produce higher levels of antibodies in a short period. In addition, this second release of antibodies tends to be more effective in binding and deactivating the antigen.

IMMUNE RESPONSE

Time (days)	*Antibody Units*
0	0
2	0
4	10
6	30
8	70
10	120
12	120
14	100
16	80
18	50
20	20
22	15
24	10
26	5
28	0
30	0
32	0
34	0
36	0
38	0
40	0
42	10
44	40
46	90
48	150
50	250
52	300
54	280
56	260
58	230
60	200

Graphing Data

Graph the following data on the axis provided below. Assume that the antigen was first introduced at time 0 and later reintroduced on day 40.



Questions

1. Describe the primary and secondary immune response in terms of: (a) speed, and (b) number of antibodies produced.

2. Which immune cells contribute to the difference in response?

Part B: Vaccination

The speed and effectiveness of the secondary immune response is the basis of vaccination. When someone is vaccinated, they are injected with a microbial antigen identified as "non-self." Although vaccinations won't cause severe disease symptoms, they will activate the primary immune response.

Some vaccinations contain dead or weakened microbes. Others contain microbe fragments. Today, vaccinations may contain genetically manufactured proteins that are identical to those found on the microbe.

Vaccination History: The Smallpox Connection

Smallpox is a devastating and deadly disease. It is caused by an infectious virus (Variola) that heavily scars skin tissue. Toward the end of the 18th century, Edward Jenner claimed that he could prevent smallpox. This English physician's claim was based upon observations of people who had recovered from cowpox. It appeared as if a bout with cowpox, a milder version of smallpox, could protect a person from getting the more severe smallpox.

In 1796, Jenner inoculated a healthy eight year old with cowpox. He later exposed the child to smallpox. To the delight of Jenner (and the boy), the child did not get smallpox. Jenner called this technique *vaccination*. We now know that cowpox and smallpox share some common proteins.

Jenner is credited with the discovery of vaccinations. However, 1,000 years earlier, the Chinese were protecting themselves against smallpox. Smallpox skin crusts were dried and inhaled. This practice produced a mild version of smallpox. This less serious illness resulted in immunity from the severe disease symptoms.

Similar practices were adopted by the Brahmins in India, the Persians, and the Turks. In 1717, Lady Mary Wortlet Montague, wife of the British Ambassador to Turkey, introduced in England the practice, called "variolation," of placing fluid from smallpox lesions into a scratch on the body of a nonimmune person. George Washington ordered his troops to be variolated in 1777.

Thanks to the improvements in vaccinations, the disease was eradicated in the world by 1977, but stocks of the virus were held for study in laboratories. In 1996, the World Health Organization voted to destroy the last samples of the virus by 1999. Until then, the United States and Russia will have stocks of variola virus.

Think About It

1. How might contemporary society react to Jenner's technique of exposing an eight-year-old child to a potentially deadly disease?
2. Do you think the last stocks of the smallpox virus should be destroyed? Why or why not?

Vaccination Survey

When you go home, discuss vaccination with your family. Ask them what kind of vaccinations they have received, for which diseases, and at what age they received the vaccination. Use their responses to fill in the table below.

Method of vaccination	Disease	Age(s) when vaccinated

Primary and Secondary Immune Response

Objective

Students graph the memory response of the immune system and read about vaccination with emphasis on its historical connections. This activity prepares students for a reading about HIV vaccines in Chapter Five.

Teacher Notes

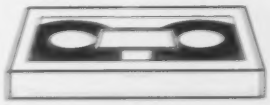
Part A: Memory Response

Survey the class to find out how many students have had chicken pox. Then ask them how many times they have had the disease. Most students will have had this disease only once. Explain that chicken pox is a disorder caused by a virus. After your body rids itself of the virus, your immune system retains a memory of the virus attack. If the virus reappears, the immune system works swiftly to rid itself of the pathogen before the virus can produce disease symptoms. This repeat defense is not only quicker, but more effective in disabling the virus.

Part B: Vaccination

Review how memory T and memory B cells heighten the secondary immune response. Then copy the following table on the chalkboard. Have students identify the vaccinations they have had. Compare and contrast the different types of vaccines. You may need to explain that inactivated viruses cannot replicate or infect cells. Weakened viruses can replicate, but do not produce severe disease symptoms. (See pages 143–145 for a more in-depth discussion.) Immunity to some microbes is longer-lived than immunity to others (chickenpox versus flu). Some diseases are caused by many different micobes (common cold).

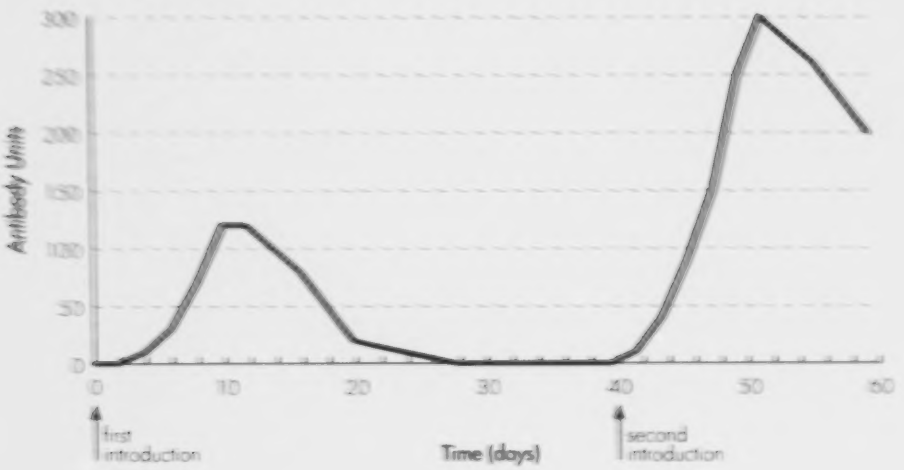
VIRUS	DISEASE	METHOD OF VACCINATION
Poliovirus	polio	Salk vaccine (inactivated virus) and Sabin vaccine (weakened virus)
Influenza virus	flu	inactivated virus
Rabies virus	rabies	inactivated virus
Hepatitis B virus	hepatitis, liver cancer	surface antigen of virus
Rubella virus	German measles	weakened virus
HIV	AIDS-related illness	none, yet



Video Connection:
See footage on retroviruses and vaccines. (22:14)

Language Connection: Have students research the derivation of the word vaccination. Suppose that the weaker pox disorder studied by Jenner affected cats. How might this have affected the name chosen for the inoculation technique?

Answers to Student Questions



Part A

1. The secondary response is swifter and produces a greater number of antibodies.
2. During a primary response, memory B and memory T cells keep a memory of the antigen. When the antigen reappears, the immune system uses this memory to mount a swifter and more effective response.

Vocabulary

primary immune response - the immune response that occurs when an antigen is recognized for the first time

secondary immune response - a more effective and swifter immune response that occurs when previously encountered antigen reappears

vaccination - an introduction of a particle, protein, or microbe that will trigger the primary immune response

HIV Infection and T Cell Counts

HIV is a virus that targets cells of the human immune system with a CD4 receptor in their cell membrane. Infected cells are eventually killed by HIV. Helper T lymphocytes (T_H) have CD4 receptors. As the T_H cell population declines, so does the person's ability to mobilize an immune response to any microbe.

When the T_H cell count drops below 500 cells per ml, the body has difficulty defending itself against certain microbes. The HIV-infected individual may begin to suffer from a number of diseases called **opportunistic infections**, such as skin rashes and fungal infections. Beneath a critical level of 200 T_H cells per ml, life-threatening illnesses, including pneumonia, tuberculosis, and cancer, may appear. At this point, the T_H-depleted individual is diagnosed with AIDS.

In this activity, you'll monitor T_H counts using drawings that represent hemacytometer fields. **Hemacytometers** are special microscope slides that are designed to be used in performing blood counts. Etched into the surface of the slide are tiny grids called counting chambers.

In order to make a blood cell count, a volume of diluted blood is placed within the counting chamber. The cells within the grid are tallied. This cell number is adjusted to reflect both the dilution and volume within the counting chamber. The final number represents the number of blood cells per 1 ml of blood. (Note: A teaspoon holds about 5 ml of fluid.)

Activity

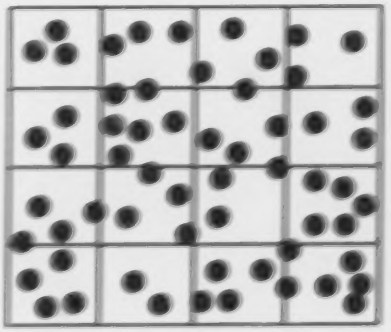
You will determine the T_H cell counts of a number of blood samples taken over time from an individual infected with HIV.

Materials

Counting chamber diagrams

Steps

1. Develop a counting pattern that is easy to remember and repeat.
2. When counting the number of cells in each box, include only the cells that lie completely within the box. You also should include cells that are touching the box's upper and right edge.
3. Count the number of red blood cells illustrated in this counting chamber. Record your results.
4. In order to calculate the number of red blood cells in 1 ml, multiply this number by 100,000. Record the numbers of red blood cells in this sample.



Hemacytometer with red blood cells

SAMPLE 1 Red Blood Cells

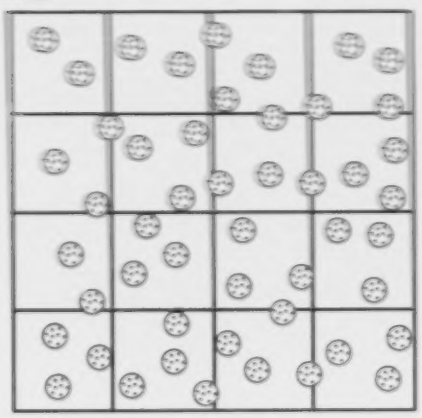
a. Number of cells in counting chamber (total) = _____

b. Number of cells in 1 ml = _____

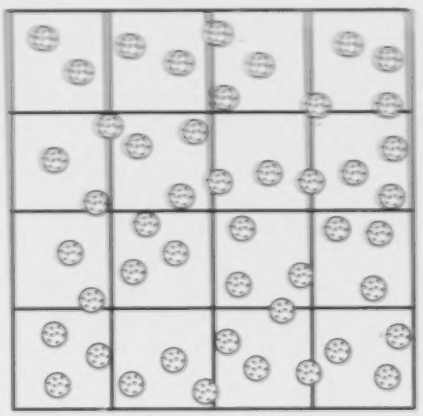
Determining T_H Cell Counts

1. The following counting chambers represent stained T_H cells measured once per year. To obtain the numbers of T_H cells in 1 ml, you'll need to multiply the cell chamber counts by 20.
2. Count and record the number of cells in each sample. Then, calculate and record the number of cells found in 1 ml of that sample's blood.

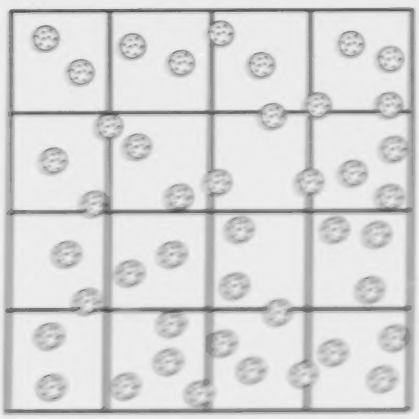
1985



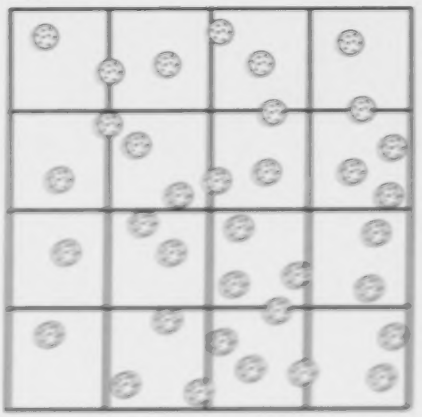
1986



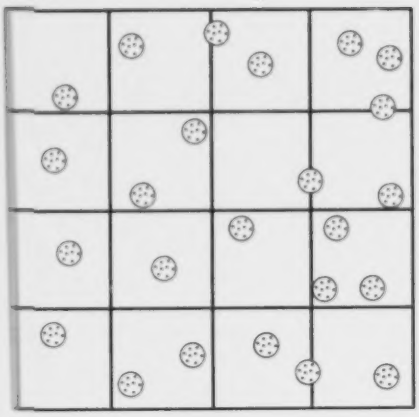
1987



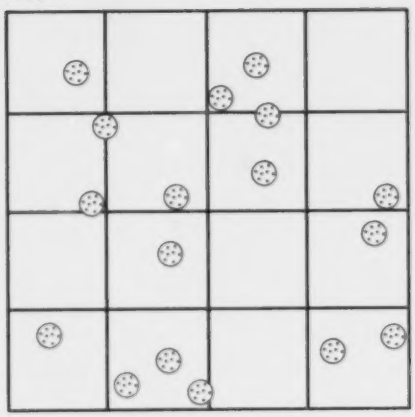
1988



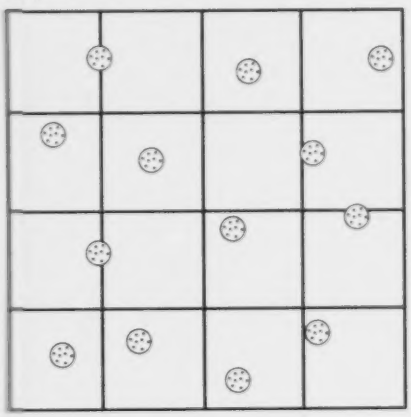
1989



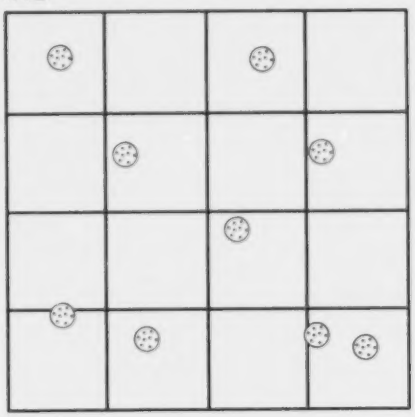
1990



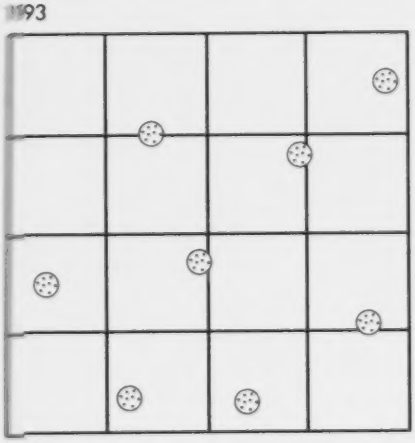
1991



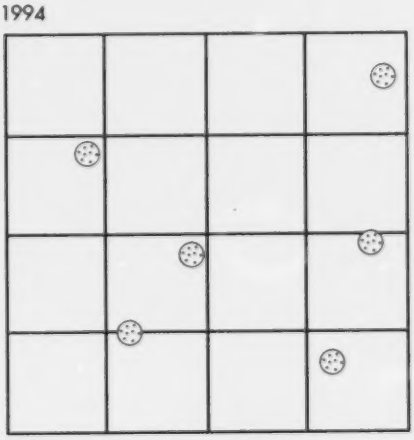
1992



1993

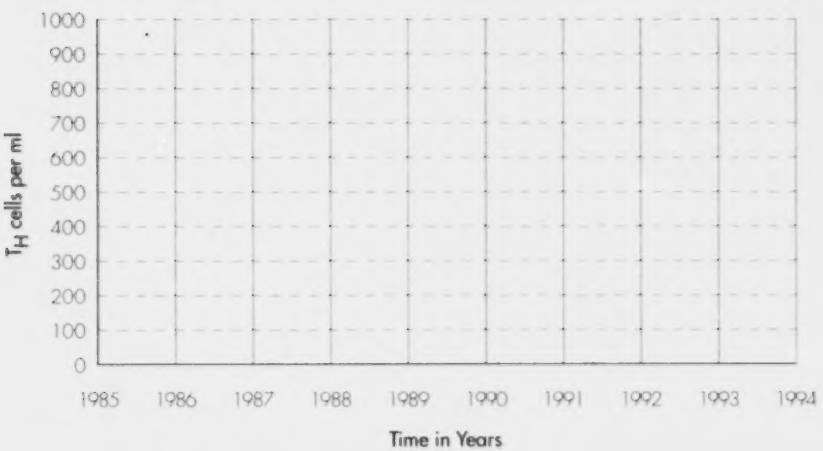


1994



T_H CELL SAMPLES	T_H CELLS IN CHAMBER	T_H CELLS PER ML
1985		
1986		
1987		
1988		
1989		
1990		
1991		
1992		
1993		
1994		

3. Use the information above to create a graph that illustrates the depletion of T_H cells during the progress of HIV infection.



4. Identify the most likely point at which opportunistic infections will begin to appear.

5. Identify the point when the HIV-infected person will be diagnosed with AIDS.

HIV Infection and T Cell Counts

Objective

Students will graph cell counts to understand the depletion of T_H cells that results from HIV infection.

Teacher Notes

Review the critical roles of the T_H cell in the immune response (page 77).

Tell students that, just like other cells, the T_H cell has protein markers on its surface. The markers of this lymphocyte are of the CD4 type. HIV envelope protein gp120 binds to CD4 proteins (see page 79, "Co-Factors in HIV-Infection"). This surface binding fuses the two membranes and allows the viral capsid to enter the host cell's cytoplasm. Within Helper T cells the viral genetic material integrates with the immune cell's DNA (forming the provirus).

When the T_H cell is presented with another antigen (such as an influenza virus or bacterial pathogen), this lymphocyte produces an altered response. Instead of releasing lymphokines, the infected cell now produces and releases new HIV virions. Eventually, the infected T_H cell dies, but it is not known how HIV kills the cell.

This depletion of T_H cells is directly responsible for the devastation of the immune response. A healthy individual has about 1,000 T_H cells per ml of blood. As the cell numbers decline, the immunity becomes increasingly compromised. At 500 cells per ml, opportunistic infections may arise. Below 200 cells per ml, the patient is diagnosed with AIDS.

BLOOD COMPONENTS

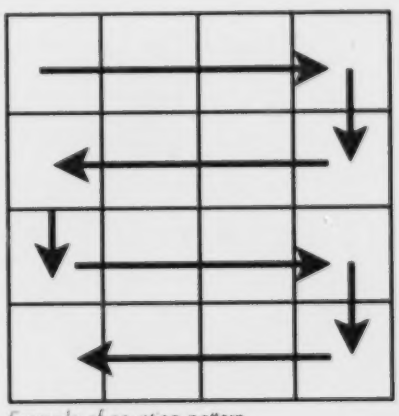
Blood consists of a liquid matrix called plasma (55 percent of the volume of the blood) and formed elements that include cells and platelets (45 percent of the volume of blood). The plasma contains dissolved salts, fibrinogen (clotting factor), immunoglobulins (antibodies), nutrients, wastes, and hormones. The breakdown of the formed elements (cells) is represented below:

Cell Type	Number *(per cc of blood)*	Function
Erythrocytes (red blood cells)	5–6 million	transport respiratory gases
Leukocytes (white blood cells)	5,000–10,000	defense and immunity
Platelets	250,000–400,000	blood clotting

Hemacytometers

If possible, have students examine an actual hemacytometer. Discuss how the use of real blood within the classroom presents a safety hazard. Also, remind students that in real blood samples there would be red blood cells and several kinds of white blood cells. The diagrams in this activity only show the T_H cells.

Review the hemacytometer counting technique. Have students discuss the advantages of counting along a pattern formed by neighboring boxes (no skips or jumps).



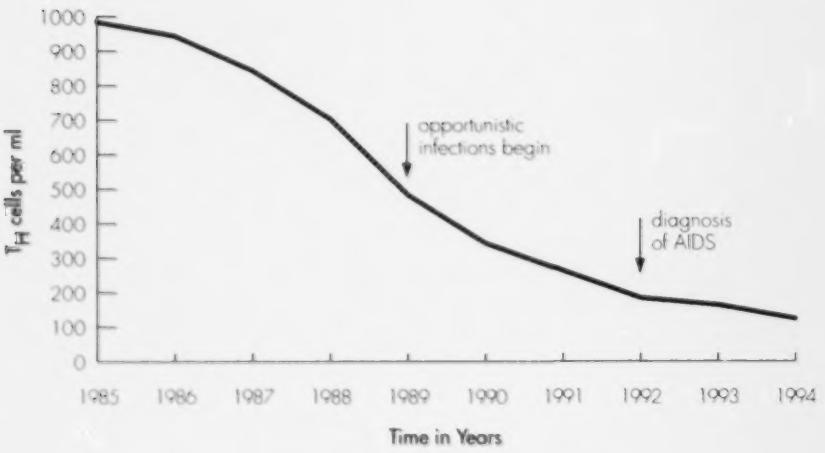
Example of counting pattern

Answers

Step 3. 60 cells

Step 4. 6,000,000 per ml

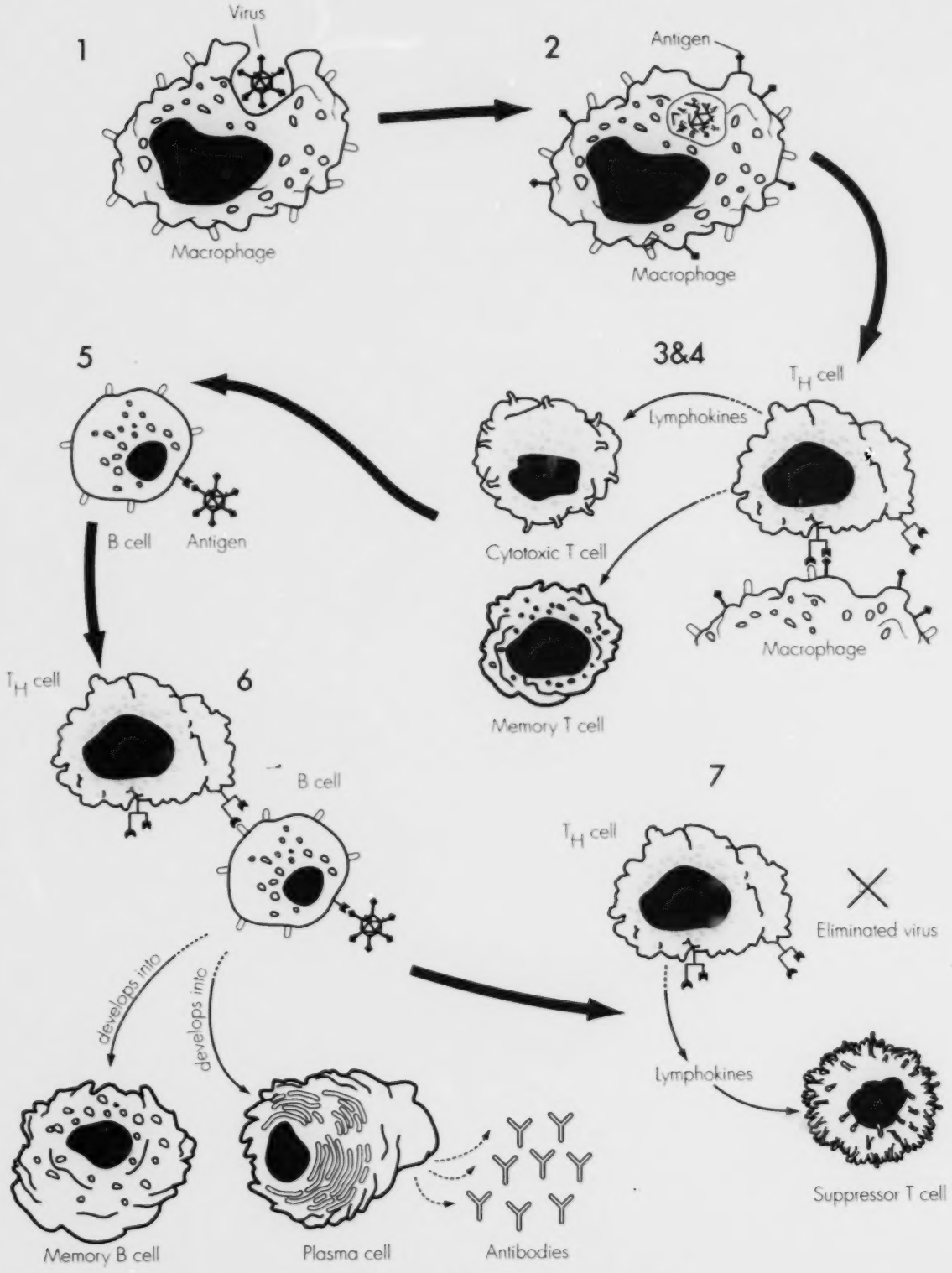
T_H CELL SAMPLES	T_H CELLS IN CHAMBER	T_H CELLS PER ML
1985	49	980
1986	47	940
1987	43	860
1988	35	700
1989	24	480
1990	17	340
1991	13	260
1992	9	180
1993	8	160
1994	6	120



Vocabulary

opportunistic infections - diseases caused by normally benign microbes or viruses that become pathogenic when the immune system is impaired

hemacytometers - special microscope slides that are designed to be used in performing blood counts



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CHAPTER FOUR

Disease Transmission

HIV Infection and AIDS

Curriculum Connections

- The Nature of Disease
- Viruses
- Monera, Protists, Fungi
- Human Immune Response
- Human Sexuality

Chapter Concepts

Chapter Four introduces the concept of disease and disease transmission. Diseases can be transmitted through casual or non-casual contacts. HIV infection requires specific contact between infected bodily fluids and either cut skin or mucous membranes to infect a person. HIV infection symptoms are not just AIDS, but a progression of disease from infection to a complete shutdown of the immune response. HIV itself does not kill the infected person. Opportunistic infections take hold once the immune response is sufficiently suppressed, and in combination these eventually cause death. HIV actually is relatively difficult to transmit, compared with some other viruses; infection can be easily prevented.

National Science Education Standards

Content Standards 9–12
Content Standard C: Matter, Energy, and Organization in Living Systems
Content Standard F: Science in Personal and Social Perspectives; Personal and Community Health
Content Standard G: History and Nature of Science; Historical Perspectives (Germ Theory)

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Types of Disease Transmission

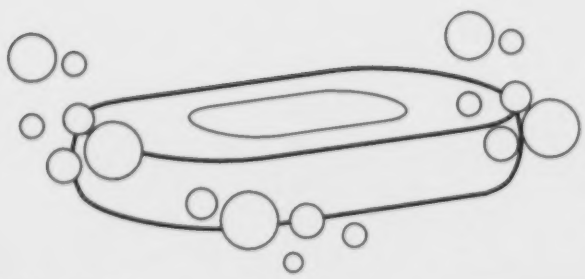
Part A: The Discovery of Infectious Disease

Ever notice how a cold seems to travel from one person to another? First, your friend gets sick. Then, your friend's sister gets sick. Next, her best friend gets sick. Eventually, half the class is suffering with the same symptoms.

When a disease outbreak affects many people, it is called an **epidemic**. The word "epidemic" comes from the Greek words meaning *common among the people*. When this "common sickness" grows to global proportions it is called a **pandemic**.

In the 16th century, most people believed that disease was spread by foul air. There were no microbes, germs, or viruses—just air that had lost its ability to keep people healthy. So strong was this belief, that the Italian phrase for bad air, *malaria*, was used to identify a common blood disease.

In 1546, a revolution occurred. In a work entitled *On Contagion*, Girolamo Francastoro proposed controversial beliefs on the spread of disease. He suggested that illness could be spread by a disease agent. Francastoro argued that air transferred unseen agents from the infected to uninfected individuals. The infection progressed into a sickness that was accompanied by disease symptoms.



Washing hands—a major medical discovery

Laboratory data backing Francastoro's work was slow to appear. It took until 1870 for Louis Pasteur to fully present his convictions on microbes and disease. Pasteur's beliefs, presented in his *Germ Theory of Disease*, implicated microbes as the cause of infectious disorders.

In the mid and late 1800s, recovery from major surgery wasn't common. Although crude surgical procedures worked, the patients often died of infections. Joseph Lister, an English surgeon, decided to improve his patients' chances for recovery by sterilizing his instruments and disinfecting his operating room. These procedures used carbolic acid and heat to destroy populations of the potentially fatal microbes. As expected, the recovery rate of Lister's patients improved dramatically.

Ignatz Semmelweis was a Hungarian contemporary of Joseph Lister. Like Lister, Semmelweis introduced the concept of sterilization and disinfection into the hospital environment. His actions were based upon the lower incidence of childbed fever in infants cared for by midwives. Semmelweis inferred that the midwives' frequent hand washing reduced the spread of disease. To improve hospital conditions, he required medical attendants to wash their hands in chlorinated lime. Although this procedure lowered the incidence of childbed fever, it wasn't popular among the staff. Semmelweis was soon dismissed from the hospital.

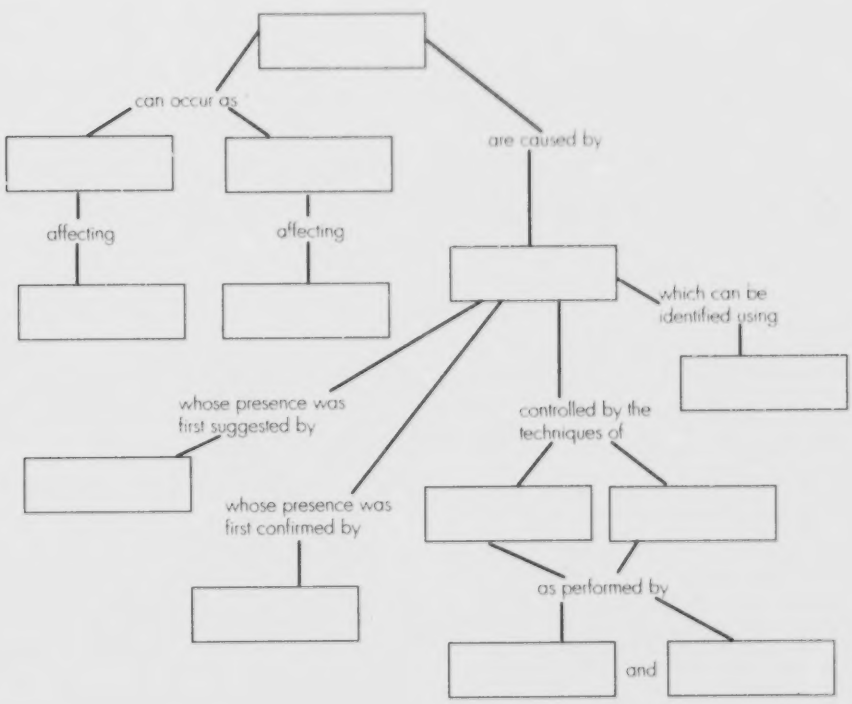
While Lister was sterilizing scalpels, and Semmelweis was washing hands, Robert Koch was studying the spread of anthrax and tuberculosis. From his observations, Koch compiled a set of postulates that would guide others in the study of infectious disease. These steps outlined the procedure for uncovering an agent of disease. These rules, which were presented formally in 1878, became known as Koch's Postulates. They state:

1. The suspect microbe must always be present in the diseased animal.
2. The suspect microbe must be isolated from the diseased animal and grown in pure culture.
3. When the microbes obtained from the pure culture are introduced into a healthy animal, the animal must become diseased.
4. Microbes from the new host must be removed and compared with the suspect original microbes to confirm its role in disease.

Questions

1. You are working in a remote region of the country. Several wild cats have died of an infectious disorder. Describe how you would use Koch's postulates to identify the causative agent of their illness.

2. Fill in the concept map using words and ideas from the section above.



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Part B: Casual or Non-Casual Contact

The flu is a common disease that comes around every winter. When you get the flu, you feel awful. This "sick feeling" is a sign of a war that rages on a cellular battlefield.

In order to "catch" the flu, you need to be infected with the influenza virus. Once inside your body, this virus replicates and destroys cells. You feel sick, feverish, and miserable. The fight between the influenza virus and immune system escalates. Over time, your defenses rally. As the virus is beaten back, your body returns to its healthful state.

Diseases like the flu are "caught" through ordinary interactions. These interactions are called casual contacts. Casual contacts include things such as eating, handshaking, and kissing. Being in the same room as someone else is also a casual contact.

Other diseases, however, do not transfer easily. Microbes that cause these diseases require special routes to get past your body defenses. Non-casual contacts provide opportunities to bypass the normal defenses.

Consider HIV. Although HIV spreads from person to person, it only can be transferred through non-casual contact. In order to become infected with HIV, the virus particles must follow a route that gets through the skin's tough, protective covering.

The chart below lists several diseases that are transferred by either casual or non-casual contact. Research the information needed to complete this chart.

Disease	Pathogen	Type of Agent	Spread by Casual or Non-Casual Contact
Influenza (flu)	orthomyxovirus	virus	casual contact
Chicken Pox			
German Measles			
AIDS			
Lyme Disease			
Measles			
Mononucleosis			
Syphilis			
Malaria			

Types of Disease Transmission

Objective

Students will read about the discovery of disease transmission and the difference between casual and non-casual contacts.

Teacher Notes

The distinction between casual and non-casual contact is important because some students may erroneously believe that HIV is spread by the same methods as other viruses, such as sneezing. HIV is only spread through specific contacts with certain bodily fluids (i.e., semen, vaginal fluids, blood, and breast milk) and cut skin or mucous membranes (see pages 110–113).

Part A: The Discovery of Infectious Disease

Several days prior to class, fill two glass flasks with a solution of chicken or beef bouillon. Before filling them, sterilize the flasks in an autoclave to prevent contamination. Place a sterile cotton plug in the mouth of one flask. Leave the mouth of the other flask unrestricted. After several days, the contents within the plugged flask should still appear clear. The contents within the unplugged flask should be cloudy with microorganisms. Explain how this activity repeated Pasteur's experiments that confirmed the association between microbe transfer and broth contamination. Instead of plugged flasks, Pasteur used swan-necked containers that trapped microbe-containing particles in their long, convoluted necks.

Part B: Casual or Non-Casual Contact

Display or wear a face mask that resembles those used in surgery. Discuss the role of this mask as a barrier that impedes the spread of infectious agents. Challenge students to compare and contrast this cloth material with the physical barrier of skin. How do these materials restrict the passage of infectious agents? How can a tear in the mask or skin compromise the effectiveness of these barriers?

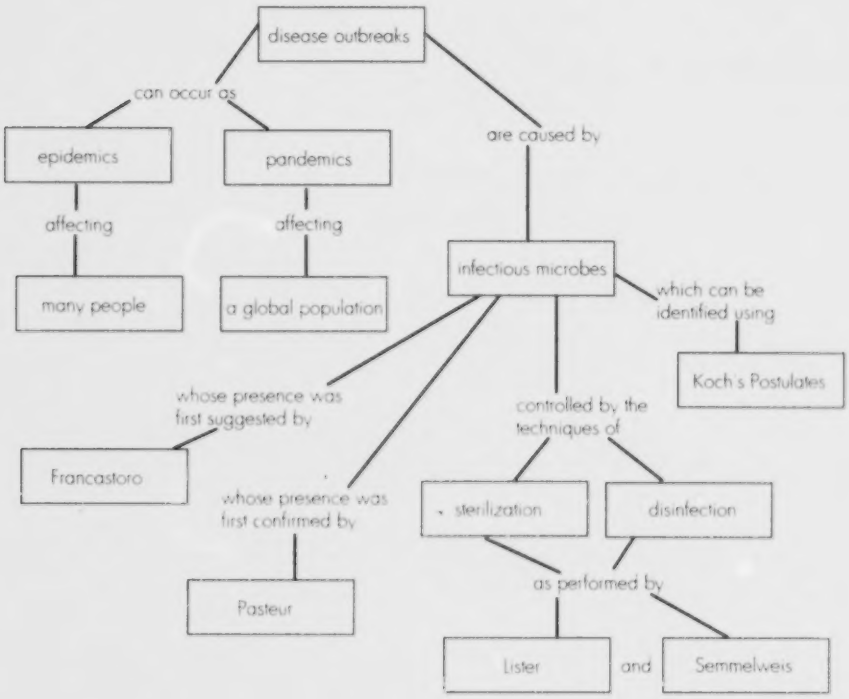
Casual contact refers to the kind of act, not the attitude one has about it. As students fill out the disease chart, explain that insect bites are listed as non-casual because the insect directly accesses the blood stream when it "bites" someone. Similarly, using a needle to inject drugs would be considered "non-casual" because the needle directly contacts the blood stream. Sexual intercourse is non-casual because mucous membranes are placed in direct contact in such a way that bodily fluids are exchanged. Kissing could be casual (peck on cheek), or non-casual (open mouth kiss). However, HIV is not spread by kissing (see pages 110–113).

Students may know that malaria, lyme disease, and some other diseases are spread by insect bites; but stress to students that HIV is *not* transmitted by insect bites.

Answers to Student Questions

Part A

1. I. Identify the likely infectious agent in the cat.
   II. Remove the agent from the cat and grow it separately in a pure culture.
   III. Inject the pure culture into a healthy cat. The healthy cat must become ill with the same disease symptoms.
   IV. Isolate the suspected agent from this newly diseased cat. Compare it with the original agent to confirm its role in disease.
2. Concept Map



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Part B

Disease	Pathogen	Type of Agent	Spread by Casual or Non-Casual Contact
Influenza (flu)	orthomyxovirus	virus	casual contact
Chicken Pox	varicella-zoster	virus	casual contact
German Measles	Rubella virus	virus	casual contact
AIDS*	Human Immunodeficiency Virus	virus	non-casual contact (sexual acts, contact with infected blood)
Lyme Disease	*Borrelia burgdorferi*	bacterium	non-casual contact (insect bite)
Measles	Morbilli virus	virus	casual contact
Mononucleosis	Epstein-Barr virus	virus	casual contact
Syphilis	*Treponema pallidum*	bacterium	non-casual contact (sexual acts)
Malaria	plasmodium	protozoa	non-casual contact (insect bite)

* *AIDS is not just one disease, but a collection of infections which occur after the primary virus (HIV) infects the body.*

Vocabulary

casual contact - everyday activities that bring people in close proximity

epidemic - disease outbreak that affects many people

non-casual contact - activities that compromise some of the body's natural defenses against infectious microbes

pandemic - epidemic of global proportions

Transmission Tracker

Think back to the last time that you were sick. Did any of your friends or family get sick, too? Was it possible to trace the spread of the sickness from one person to another?

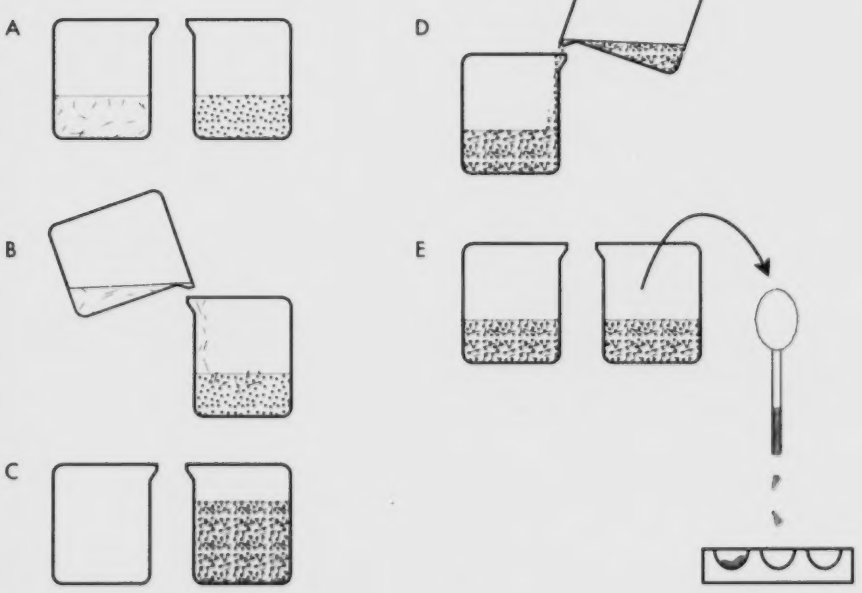
In this activity, you take on the responsibility of an **epidemiologist**. Your assignment is to uncover the pattern followed by a spreading chemical marker. But before you can analyze the data, you'll have to participate as one of the possible carriers.

Materials

multiwell plate (or four test tubes)
small beaker (containing unknown solution)
medicine dropper with bulb
phenolphthalein indicator solution

Steps

1. Examine the unknown sample supplied by your instructor. (The liquid is an irritant. Do not touch, taste, or smell the solution.)
2. Use the dropper to place about 10 drops of the unknown solution into well #1 of a multiwell plate (or test tube #1).
3. (a) Identify an exchange partner. (b) Mix the contents of the two beakers. (c) Swirl the mixture. (d) Return half the mixture into the empty beaker. (e) Place about 10 drops of your new solution mixture into well #2. Record the name of the first exchange partner in the table provided.
4. Identify a different exchange partner. Exchange liquids as you did in step 3. Place about 10 drops of the newly mixed beaker contents into well #3. Record the name of the second exchange partner.
5. Repeat step 4 two more times. Record the names of the third and fourth exchange partners.



6. Exchange liquid with one more partner. Do not pour off any of the mixture. Instead, add several drops of phenolphthalein solution to the beaker contents. Swirl the mixture. Record the name of the exchange partner. Compare your beaker with the beakers of other students. Record the color of your beaker's final solution in the table below.
7. Add several drops of phenolphthalein solution to each of the well contents. Record your results below.

SOLUTION TESTED	EXCHANGE PARTNER	COLOR CHANGE (YES/NO)
Well #1	none	_____
Well #2	_____	_____
Well #3	_____	_____
Well #4	_____	_____
Final mixture (in beaker)	_____	_____

Questions

1. What was the purpose of the phenolphthalein solution?

2. Was your final mixture "infected"? How did you tell?

3. How could you tell when a solution became infected with the chemical marker?

4. Compile and analyze the classroom data. Describe how this infection was spread.

Transmission Tracker

Objective

Students will simulate the spread of disease and the way epidemiologists track disease transmission.

Teacher Notes

Materials (for a class of 30)

30 multiwell plates (or 120 test tubes or small cups)
30 small beakers or cups
classroom set of dropper bottles containing phenolphthalein indicator solution
30 medicine droppers with bulbs

Safety

Remind students that the liquid they are transferring is a corrosive base. Supply students with goggles and review laboratory procedures for handling, transferring, and working with corrosive solutions.

Preparation

Produce a diluted sodium hydroxide (NaOH) solution by adding 25 ml of concentrated NaOH solution (or dissolve 2 grams of NaOH) to 0.5 liters of distilled water. Mix well. Prior to class, fill three small beakers about one-third full with the diluted NaOH solution. Fill the remaining classroom set of beakers to about the same level with distilled water.

Distribute protective eye-wear and inform the class that the solution can irritate skin. Then, randomly distribute the beakers. Each student should receive only one beaker.

Have the students follow the directions presented on the hand-out sheets. Encourage the students to mingle and exchange liquids with students from the far side of the room.

After the wells have been analyzed for the presence of the infectious agent, compile the classroom data. Explain that the unknown contaminated liquid was a dilute NaOH solution. When mixed with the alkaline indicator phenolphthalein, the solution turns pink. Have students discuss how this observation can be used to track the spread of the contaminated solutions. Challenge the class to reconstruct the exact path of NaOH transfer.

Discuss the kind of contact the exchanges could represent. If exchanging liquid is sneezing, that would be a casual contact. If exchanging liquids represents sexual intercourse, that would be non-casual contact.

Answers to Student Questions

1. To test for the presence of the infectious agent (NaOH)
2. Answers will vary. A color change identifies an "infected" solution.
3. When mixed with the indicator, it turned pink.
4. By analyzing the pattern of fluid exchanges that resulted in infection, students will be able to uncover how the marker was spread.

Vocabulary

epidemiologist - scientist who studies the spread and transmission of disease in human populations

phenolphthalein - indicator solution that turns pink in the presence of a base

Emergence of the HIV Epidemic

In the Transmission Tracker activity, you traced the histories of you and your exchange partners. By uncovering the route of infection, you were able to uncover how the agent was spread. But suppose you hadn't recorded or tested each exchange? How could this affect tracking the spread of an unseen agent?

In the early 1980s, scientists faced a difficult task. An illness with no previous history swiftly emerged in major population centers in the United States. The very agent that produced this disorder could not be uncovered.

The first reported cases of this outbreak involved several young men with respiratory problems. These patients were suffering with PCP, a type of pneumonia produced by the fungus **Pneumocystis carinii**. Normally kept under control, this fungus now flourished in the patients' bodies with deadly consequences.

Other emerging symptoms included dark brown and purple skin splotches. These bruise-like discolorations were tumors of blood vessels in the skin. They were produced by a type of cancer called **Kaposi's sarcoma**.

Prior to these outbreaks, Kaposi's sarcoma appeared mostly in elderly men of East European and Italian heritage. This new form targeted much younger men from a variety of ethnic backgrounds. In addition, the tumors were unusually aggressive. They spread quickly. Often the cancer invaded deeper tissues and lymph nodes. Many of the Kaposi's sarcoma patients were simultaneously subject to other microbial infections.

Counts of white blood cells in the affected men confirmed what doctors had suspected. They didn't have enough immune cells to fight off infection. The lack of defense cells opened the door to a variety of life-threatening infections and cancers. The set of symptoms was called **Acquired Immune Deficiency Syndrome**, or **AIDS**.

As more cases were reported, the outbreak's pattern emerged. Most of the AIDS patients were sexually active gay men. At first, some physicians suggested that the immune system was destroyed by the introduction of foreign sperm. Others felt that the defenses were damaged by harmful, recreational drugs. The outbreak escalated. As more information was gathered, scientists abandoned these early speculations.

In 1982, AIDS-like symptoms appeared in a six-month-old infant. The records revealed that the child had received a blood transfusion. Within two years, one of the infant's blood donors developed AIDS. It appeared that AIDS also was transferred through infected blood.

Epidemiologists realized that a blood connection also would account for AIDS in intravenous drug abusers. Through sharing needles, I.V. drug abusers spread blood diseases among themselves. The spread of AIDS was behaving like that of other blood-borne pathogens.

The blood route was confirmed when AIDS surfaced in a sharply defined population—hemophiliacs. Suffering from hemophilia, an inherited blood disease, these individuals required blood products to control bleeding. Most likely, hemophiliacs became infected with the AIDS pathogen that contaminated the blood and blood products. Since processed blood products had passed through bacteria-catching filters, something smaller was suspected. The search for an AIDS virus began.

In 1983, the Human Immunodeficiency Virus (HIV) was independently identified by Luc Montagnier in France and Robert Gallo in the United States.

Timeline of HIV discovery and treatments

1981:	First reported cases in U.S. of young men suffering from PCP
1982:	Symptoms appear in an infant and in hemophiliacs. Disease symptoms called AIDS
1983:	Identification of HIV
1985:	First antibody test for HIV in U.S.
1987:	AZT approved by U.S. FDA
1996:	Protease inhibitors show success as a therapy; p24 antigen tests approved by U.S. FDA for blood screening

Questions

1. What is Kaposi's sarcoma?

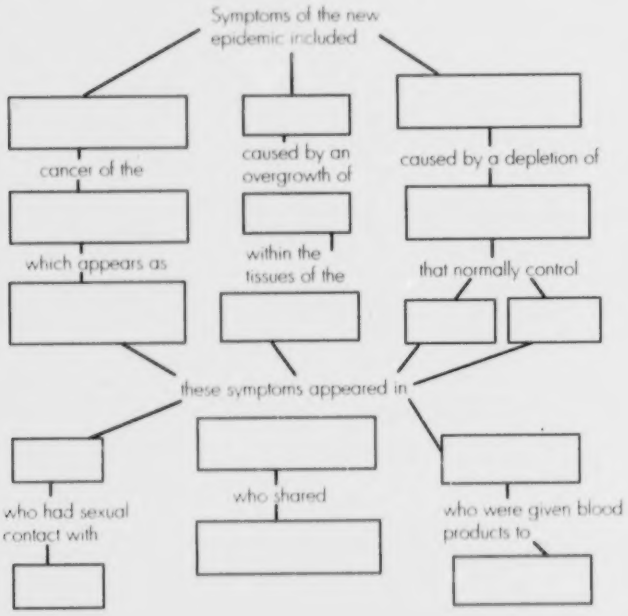
2. Describe two ways in which the emerging Kaposi's sarcoma epidemic differed from the classic cases of this disorder.

3. Why was the growth of *Pneumocystis carinii* unchecked by the body's defenses?

4. Name three groups of people in which the symptoms of AIDS were first identified.

5. What led investigators to believe that AIDS was caused by a blood-borne virus?

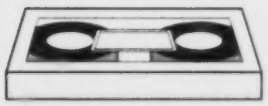
6. Fill in the concept map using words and ideas from the section above.


Symptoms of the new epidemic included
cancer of the
caused by an overgrowth of
caused by a depletion of
which appears as
within the tissues of the
that normally control
these symptoms appeared in
who had sexual contact with
who shared
who were given blood products to

Emergence of the HIV Epidemic

Objective

Students will read the early history of the HIV/AIDS epidemic in the United States. However, students should understand that HIV has spread throughout the world; the exact origin is unknown.



Video Connection:
See television news clips from 1982. Dr. Fauci also discusses some history of the epidemic. (14:57)

Teacher Notes

Display a large beaker filled with water. Add a drop of food coloring without stirring and have students observe the diffusion of the dye. Compare and contrast the diffusion of this chemical with the spread of an infectious agent. Challenge students to compile a list of factors that would affect the spread of an infectious disease.

Stress to students that, since HIV has been identified, blood supplies in the United States are screened for the virus and are safe. The HIV tests and treatments in the timeline on page 106 show students that progress has been made since the virus was first identified.

THE ORIGINS OF HIV: SOME THEORIES

One theory on the origin of HIV states that HIV has been infecting humans for thousands of years. During that time, the epidemics were limited and did not extend beyond isolated villages. Modern travel, however, brought the virus to many more groups of people, and it spread widely.

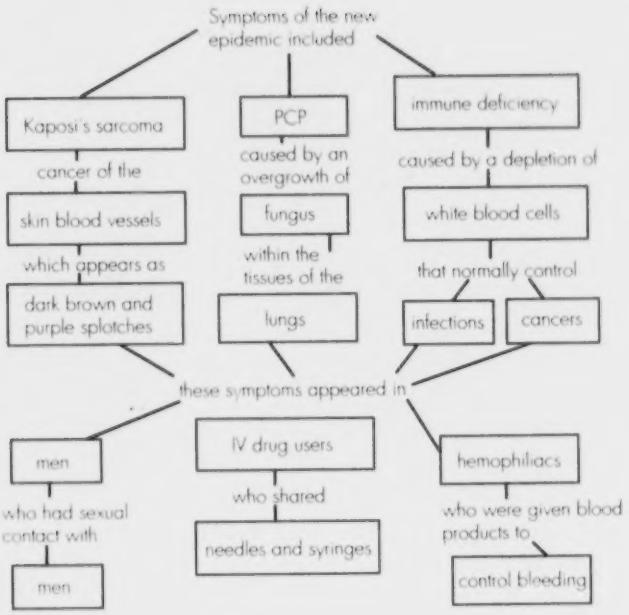
A related theory suggests that HIV may be a human virus that only recently became deadly. People may have been infected with a milder form of HIV but had few, if any, symptoms. Suddenly, a mutation turned the virus into the deadly HIV. People infected with this strain left their local area and transmitted the virus to other groups of people.

Some African monkey populations are infected with a simian retrovirus (Simian Immunodeficiency Virus, or SIV) with similarities to HIV-2. When introduced into healthy monkeys, the SIV produces AIDS-like symptoms. SIV's genome is similar to that of HIV-2, suggesting that HIV-2 and SIV are related. Since both viruses resemble other simian viruses, it is likely that HIV-2 was initially a monkey virus. Sometime in the past, the virus jumped host to humans.

Answers to Student Questions

1. It is a cancer of blood vessels in the skin.
2. It infected young victims. It was more virulent than classic KS.
3. There were too few immune cells to control its population.
4. Gay men; I.V. drug abusers; hemophiliacs (blood transfusion recipients)
5. The spread of infection suggested a blood-borne pathogen. Filters would have prevented bacteria and larger pathogens from being transferred.

6. Concept Map



Vocabulary

Acquired Immune Deficiency Syndrome (AIDS) - a set of symptoms that appear during the late stages of HIV infection

hemophilia - an inherited blood disease in which blood lacks a clotting factor

Kaposi's sarcoma - a cancer that affects blood vessels of the skin

Pneumocystis carinii - a parasitic fungi that causes pneumonia

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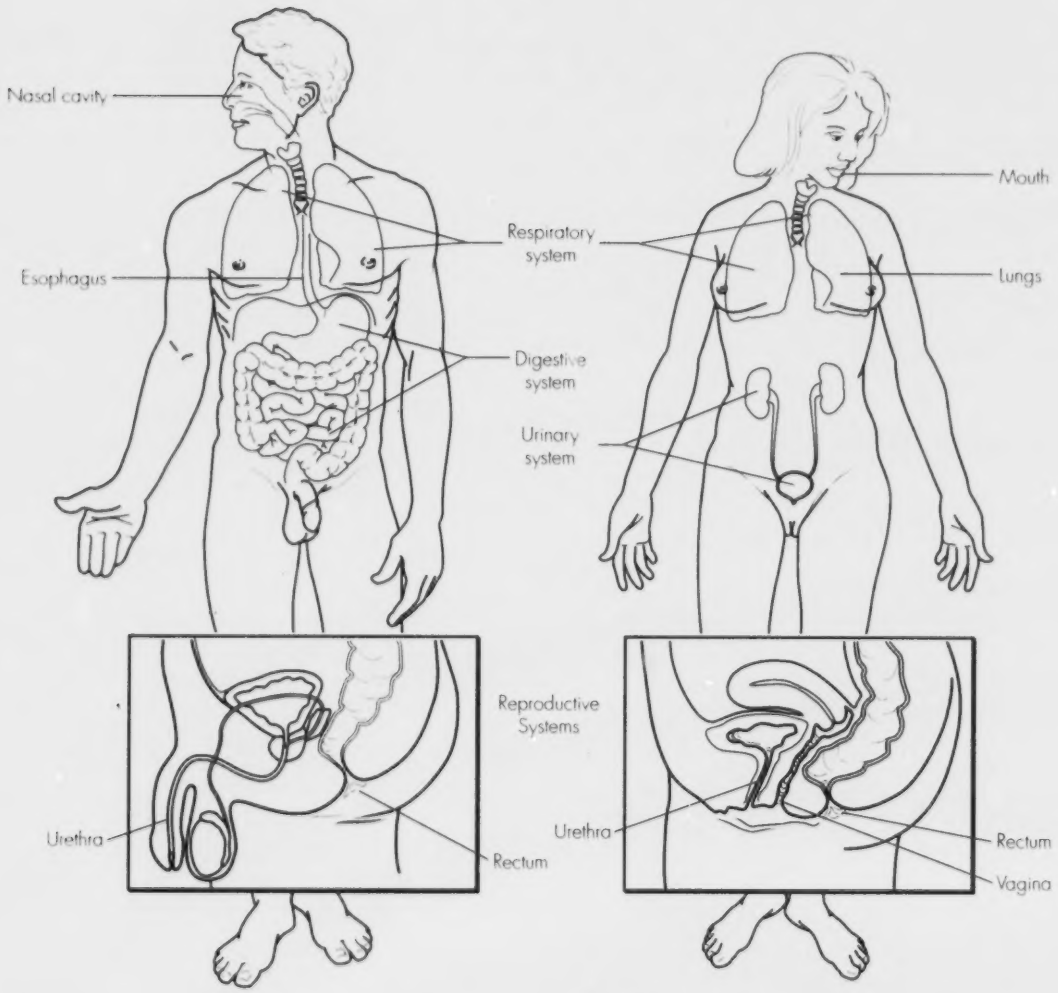
A Compromised Barrier

HIV Transmission

Skin is a tough, physical barrier. Wherever this living armor remains intact, it blocks HIV from getting into the body. This coverage, however, is not flawless. Skin can be torn, scraped, ripped, or punctured.

In order to become infected with HIV, the virus must get through your skin's thick barricade of cells. This isn't an easy task. HIV cannot be transferred by hugging, shaking hands, coughing, nose blowing, or sharing towels. All of these activities do not compromise the defense capability of the skin. Intact skin does its job and keeps HIV out. HIV is also fragile; it cannot withstand exposure to air or water. Without the protective surroundings of body tissues and body fluids, HIV disintegrates.

The linings of the respiratory, urinary, digestive and reproductive systems do not have a thickened barricade of skin cells. Instead they are covered by a moist **mucous membrane**. These membranes are specialized to secrete or absorb materials. Mucous membranes can



develop small tears in them more easily than regular skin. In addition, these surfaces have many CD4-presenting macrophages. HIV that comes in contact with these cells can infect them without first entering the blood. Common ways HIV enters the body are through the vagina, rectum, urethra (male), and mouth.

Even if an HIV particle gets into a person, the particle may not establish infection. In order to become HIV infected, you need to receive a sufficient dose of viruses. If too few viruses enter your body, they may be eliminated by your immune response.

A cut, scrape, or puncture wound offers a route through which HIV may pass. **Hypodermic needles** and **syringes** are very effective in transferring HIV. Not only do the needles breach the skin defense, but a sufficient dose of HIV is easily contained within a syringe.

In an HIV-infected person, viruses are not equally distributed in body fluids and tissues. HIV is present in the cells (T_H cells and macrophages) of **blood**, **semen**, and **vaginal fluid.** Scientists have determined that these fluids contain enough HIV to infect another person. **Breast milk** also contains HIV; infected mothers may transmit HIV to their babies during breastfeeding.

Questions

1. What happens when HIV is exposed directly to air or water?
2. Can HIV be spread by non-infected body fluids? Explain.
3. Must every contact with infected fluid lead to the HIV infection? Explain.
4. Examine the two lists below. How can the body fluids (that contain enough HIV to infect a person) be combined with the entry points to transmit HIV?

HIV-Infectious Body Fluids	HIV Entry Points
▪ Blood (includes blood from cuts and menstrual blood)	▪ Cut skin or needle puncture
▪ Semen	▪ Rectum
▪ Vaginal fluids	▪ Vagina
▪ Breast milk	▪ Lining of male urethra (penis)
	▪ Mouth

A Compromised Barrier

HIV Transmission

Objective

Students will discuss ways that infected bodily fluids (that contain a high enough concentration of HIV to infect another person) can contact cut or punctured skin or mucous membranes to transmit HIV. By knowing how exactly HIV is transmitted, students can understand how to prevent infection.

Teacher Notes

Review the defense role of the skin. Explain how HIV can gain entrance to the body if the skin barrier is compromised (cut, punctured). Discuss how mucous membranes are more easily torn than regular skin (e.g., skin on one's arms and legs).

The three major routes of HIV infection are: (a) sex acts, (b) blood contact (injection by contaminated needle, infected blood on open cuts), and (c) mother to fetus in utero, during birth, or breastfeeding. **Worldwide, the predominant method by which HIV is transmitted is sexual fluids (semen and vaginal fluids) contacting mucosal surfaces (mouth, vagina, lining of male urethra, rectum).**

Blood, semen, vaginal fluids, and breast milk are not the only body fluids which contain HIV. But they are the fluids which contain high enough concentrations to infect another person with HIV. Remind students that "blood" also means menstrual blood and tissues.

HIV is not spread by tears, sweat, coughing, or sneezing. HIV is not transmitted by insect bites.

If appropriate, challenge the students to describe the biological nature of the skin barrier compromise associated with the following transmission routes:

a. blood transfusions (with HIV-infected blood)
b. I.V. needle and syringe sharing
c. penis in anus
d. penis in vagina
e. oral sex (mouth on penis, mouth on vaginal opening)
f. sexual fluids on open cuts
g. infected blood on an open cut
h. nursing mothers
i. fetal and birth events

HIV TRANSMISSION

HIV-Infectious Body Fluids	HIV Entry Points
■ Blood (including menstrual blood)	■ Cut/punctured skin
■ Semen	■ Rectum
■ Vaginal fluids	■ Vagina
■ Breast milk	■ Lining of male urethra (penis)
	■ Mouth

These two lists are in order of infection potential. In other words, HIV-infected blood and semen have higher concentrations of HIV than infected vaginal fluids and breast milk, and thus have a greater probability of infecting a person. Similarly, the rectum and vagina are more likely to be infected than the male urethra or the mouth. The rectum has a very thin wall and may be easily torn. The vagina contains macrophages that can be infected with HIV, and the vagina may also be slightly torn during sexual intercourse. Remind students that even before a man ejaculates semen, pre-ejaculatory fluid is present which contains HIV, albeit in low concentrations. Stress to students that any contact between infected body fluids and the mucous membranes listed may result in HIV infection.

INSECT TRANSMISSION

Students are often concerned about the spread of HIV by insects. To date, there have been no proven cases of insect transmitted HIV. In places such as Zaire, where insect bites are common, children living in the households of HIV-infected individuals have not become infected.

Answers to Student Questions

1. The virus breaks down.
2. No, in order to be infective, the body fluid must contain the virus.
3. No, although a single virus can establish infection, it is unlikely. A sufficient viral load is needed to establish infection.
4. Methods of HIV transmission include sex acts and infectious fluids contacting cut skin or introduced through a needle.

Vocabulary

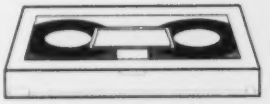
hypodermic needle - a sharp, hollow point needle used to puncture the skin

mucous membrane - lining of urinary, reproductive, digestive, and respiratory systems; examples are the mouth, vagina, urethra, and rectum

semen - fluid that contains sperm and secretions from the male reproductive glands

syringe - a chamber that holds, injects, or draws out fluids

vaginal fluid - fluid that contains secretions from the female reproductive organs



Video Connection:
Several of the young people in the video explain how they were infected with HIV.

The Progression of HIV Infection

The progression of HIV infection varies widely from person to person. Some people, though rare, will die from HIV-related illnesses within months. Most will harbor the virus for years showing few signs of infection. Researchers believe that many factors affect the course of this illness. Such factors include the strain of HIV, the individual's genes, previous disorders, and the state of the immune system. Since everyone is different, the disease progression in each individual will be different.

Even so, some patterns do arise. These patterns are used to divide HIV infection into events and stages. Although many people may progress according to these patterns, many will not. The susceptibility, symptoms, stages, progression, and outcome of HIV disease vary widely from person to person.

The initial exposure to HIV occurs when a person who does not have the virus is exposed to an infectious dose of the virus. HIV that escapes immune action then establishes a permanent infection.

STAGE ONE Initial Infection Period

During this period, the virus rapidly replicates. New HIV particles flood the blood stream and lymphatic system. As they travel freely through the body, the virus particles disperse and may establish infections in T_H cells, lymph tissues, nodes, and various organs.

Some people experience no outward symptoms during the early phase of infection. Others develop a flu-like illness. The onset of these symptoms (fever, headache, and swollen lymph nodes) usually occurs three to eight weeks after infection. They may last for weeks, then subside.

During this period, the immune system recognizes and targets HIV. B cells produce antibodies specific to this virus. The appearance of HIV antibodies in the blood signals a blood chemistry change called **seroconversion.** From this time onward, the blood will contain a chemical record of the HIV infection.

STAGE TWO Asymptomatic Stage

Although there may be few outward symptoms, HIV remains active. It continually replicates and infects healthy cells. During this stage, the lymph nodes contain many viruses where they contact and infect high numbers of T_H cells.

Throughout this destruction, the lymph glands may swell periodically. Deep within the lymph tissues, a war rages. It is a battle of attrition. Viruses and T_H cells are destroyed. But unlike their viral attackers, the T_H cells cannot be fully replaced. Their population enters a period of decline.

The asymptomatic stage may be as short as six months, or last well over 10 years.

STAGE THREE Swollen Lymph Node Stage

This stage is characterized by the persistent swelling of the lymph nodes. The nodes of the groin, neck, and armpits may remain swollen for up to six months. During this time, the immune cells in the lymph nodes are slowly being destroyed.

In some cases, this swelling is accompanied by other symptoms of disease including weight loss, fever, and fatigue.

STAGE FOUR Chronic Disease Stage

In the continuing battle, both viruses and immune cells are being destroyed. The balance, however, has now shifted in favor of the virus.

As the body's T_H cells become depleted, he or she begins to develop outward signs of HIV infection. These symptoms may include fever, weight loss, night sweats, diarrhea, malaise, pain, headaches, and swollen lymph glands.

Eventually, the structure of the lymph nodes falls apart. Large numbers of viruses flood the bloodstream. With the decline of lymph and T cell defenses, **opportunistic infections** and cancers arise.

STAGE FIVE AIDS

When the T_H cells drop below a critical level, HIV infection has reached its most severe form—AIDS. Currently, AIDS is diagnosed in patients who have less than 200 T_H cells per ml of blood or symptoms of specific illnesses. In most patients, this depletion is accompanied by life-threatening infections, rapidly spreading tumors, and extreme loss of weight (wasting syndrome). But remember, all stages of HIV disease, including AIDS, vary widely from person to person. Some HIV-infected individuals with T_H counts below 200 cells per ml remain free of life-threatening infections. In contrast, others with much higher T_H cell counts succumb to AIDS-related illnesses.

Charting Disease Progression

Use the descriptions of the fictional case histories below to mark each patient's time line as instructed.

PATIENT A	PATIENT B	PATIENT C	PATIENT D
▪ HIV antibodies appear six weeks after initial infection	▪ HIV antibodies appear three weeks after initial infection	▪ HIV antibodies appear 10 weeks after initial infection	▪ HIV antibodies appear two weeks after initial infection
▪ Has flu-like symptoms from weeks two through four	▪ Has flu-like symptoms for one week following antibody appearance	▪ Has no flu-like symptoms	▪ Has no flu-like symptoms
▪ Persistent lymph gland swelling for two months starting at nine years	▪ Has no persistent lymph gland swelling	▪ Persistent lymph gland swelling for six months starting at seven years	▪ Has no persistent lymph gland swelling
▪ T_H cell count drops below 500 at six years	▪ T_H cell count drops below 500 at one year	▪ T_H cell count drops below 500 at seven years	▪ T_H cell count never drops
▪ Minor opportunistic infections begin at seven years	▪ T_H cell count drops below 200 at two years	▪ T_H cell count drops below 200 at eight years	▪ Opportunistic infections not observed during the period of study
▪ T_H cell count drops below 200 at ten years	▪ Severe opportunistic infections begin at two years	▪ Opportunistic infections not observed during the period of study	
▪ Severe opportunistic infections begin at 11 years	▪ Succumbs to opportunistic infections at three years		
▪ Succumbs to opportunistic infections at 12 years			

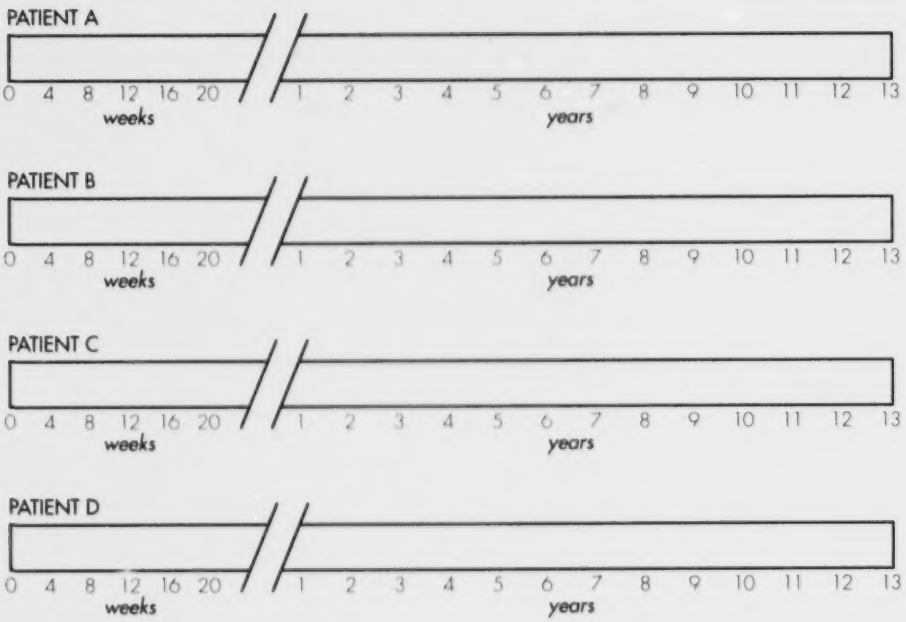
1. Fill the time period between the initial infection and the first detected antibodies with a dotted texture.

2. Identify the first T_H cell counts of 500 and 200 with the terms "500 T_H cells per ml" and "200 T_H cells per ml."

3. Fill in the period between the 500 and 200 T_H cell count with a diagonal line pattern.

4. Fill in the period in which the T_H count is below 200 with a solid shade.

Compare and contrast the completed time lines. How is the progress of HIV infection similar? How is it different?



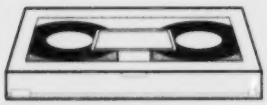
Infection to when antibodies appear

500–200 T_H cells per ml

Below 200 T_H cells per ml

130

The Progression of HIV Infection



Video Connection:
The HIV-infected young people in the video mention different disease symptoms.

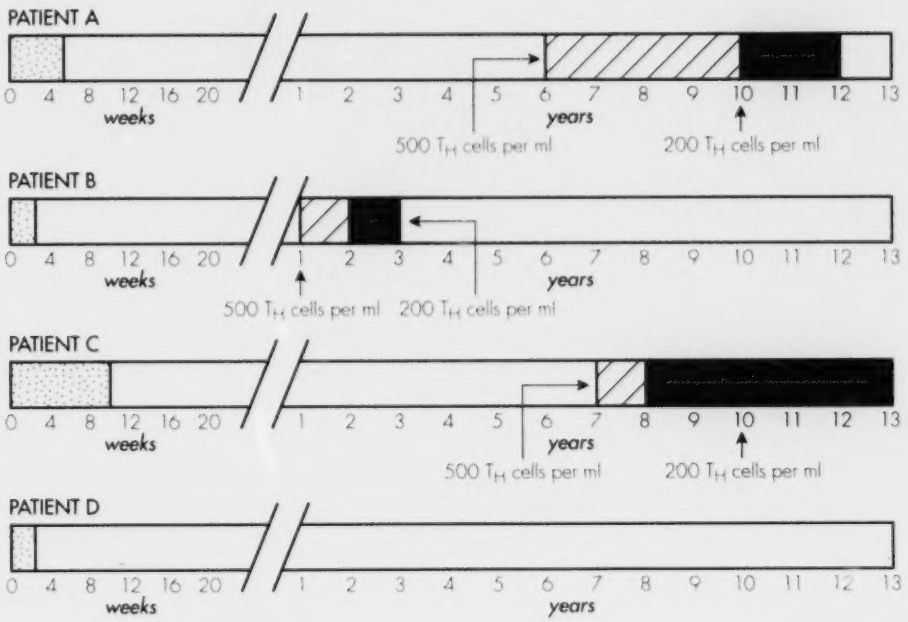
Objective

Students graph fictional examples of the progression of HIV infection to understand the variability of effects from person to person.

Teacher Notes

Explain that the progression and symptoms of HIV disease vary from person to person. Some people succumb to the opportunistic infections within a year. Others can remain infected but show no immune dysfunction for more than 15 years. Even so, researchers have identified stages that are common to many cases.

Answers to Student Questions


PATIENT A
0 4 8 12 16 20 1 2 3 4 5 6 7 8 9 10 11 12 13
weeks
years
500 T_H cells per ml
200 T_H cells per ml
PATIENT B
0 4 8 12 16 20 1 2 3 4 5 6 7 8 9 10 11 12 13
weeks
years
500 T_H cells per ml
200 T_H cells per ml
PATIENT C
0 4 8 12 16 20 1 2 3 4 5 6 7 8 9 10 11 12 13
weeks
years
500 T_H cells per ml
200 T_H cells per ml
PATIENT D
0 4 8 12 16 20 1 2 3 4 5 6 7 8 9 10 11 12 13
weeks
years

Vocabulary

asymptomatic - without symptoms

opportunistic infection - infection that flourishes in response to growth opportunities

seroconversion - appearance of specific antibodies in the blood

Symptoms of Infection

Part A: Opportunistic Infections

Your body is home to all sorts of microscopic organisms. For the most part, they aren't bothersome. Their numbers are too small to harm you. Some are even helpful.

If one of these populations swells, your immune system acts swiftly. It trims the population back to an acceptable and manageable size. This immune response is coordinated by the T_H cell. Under the watch of a healthy T_H count, dangerous microbes are continually cut back.

During HIV infection, things change. T_H cells are targeted and destroyed. Their declining numbers are overwhelmed by the resident microbes. Organisms and viruses that were once kept in check, now multiply freely. Their growth produces a variety of disorders called **opportunistic infections** (OIs). It is the OIs, not the drop in T_H cells, that kill the person infected with HIV.

Not every person infected with HIV suffers from every OI. Generally, however, the first OIs to appear affect the skin. Surface bacteria produce skin infections. The latent chicken pox virus reactivates. Its unchecked replication produces new skin symptoms called **shingles**.

The next round often involves two fungal parasites. *Candida albicans* may grow on the surface of the tongue, mouth, throat, and vagina, producing a thick coating called thrush. At the same time, the fungus that causes athlete's foot, *Trichophyton*, (a non specific type of athlete's foot) rages uncontrollably.

At this time, most infected people will show signs of weight loss. Over time, this tendency to lose weight will progress to a severe "wasting syndrome." Recurring fevers called "night sweats" begin.

Usually when the T_H cell count drops below 200 cells per ml, a horde of even deadlier pathogens arise. One of these microbes is the fungus *Pneumocystis carinii*. No longer under the control of the immune system, *P. carinii* devastates lung tissue. Its deadly carnage accounts for most AIDS-related deaths.

"Keying Out" Opportunistic Organisms

Scientists often identify an unknown organism by using a taxonomic key which is a list of paired statements. As you agree or disagree with the statements in a key, you are directed to the next, most appropriate statement pair. By navigating a custom path, you wind up at the name of the unknown organism. Here's your chance to use a key. The statements in the box describe a variety of opportunitic organisms that flourish during the later stages of HIV infection. Use the key to uncover the identity of each pathogen.

OPPORTUNISTIC ORGANISMS

1. **FUNGUS:** affects mucous membranes of the mouth, esophagus, anus, and vagina; infection often occurs when T_H cell count falls to between 200–300 cells per ml; its characteristic white patches may be first symptom of opportunistic infection
2. **VIRUS:** member of the herpes virus family; tends to infect the retina of eyes, eventually producing blindness; produces broad spectrum of symptoms affecting endocrine, respiratory, and digestive systems; causes severe diarrhea, fever, and anemia
3. **PROTOZOAN:** infects a wide variety of animals; targets brain, producing tissue damage including tumors and abscesses; can be transmitted by domestic cats
4. **FUNGUS:** affects lung tissue; leading cause of AIDS-related deaths; symptoms include a dry cough and shortness of breath; produces an often deadly condition known as Pneumocystis carinii pneumonia (PCP).
5. **BACTERIUM:** spread mostly by infected airborne droplets; infects the lungs; spreads throughout chest cavity; leading pathogen of bacteria-caused death

KEY TO IDENTIFY OPPORTUNISTIC ORGANISMS

1a. Opportunistic pathogen is a virus	2
1b. Opportunistic pathogen is an organism	4
2a. Targets lymph nodes, produces tumors	**Epstein-Barr virus**
2b. Targets tissues other than lymph nodes	3
3a. Targets a variety of organ systems; infection of the retina often leads to blindness	**Cytomegalovirus (CMV)**
3b. Targets mucous membranes causing blisters and ulcers	**Herpes simplex**
4a. Organism is fungus	5
4a. Organism is a protozoa or bacteria	8
5a. Produces oral thrush; severe and painful irritations of the vagina and esophagus	***Candida albicans***
5b. Targets lungs; and may or may not involve other tissues	6
6a. Targets primarily lung tissue	***Pneumocystis carinii***
6b. Targets lungs and other body systems	7
7a. Attack may involve the liver, lymph nodes, and nervous system	***Histoplasmosis capsulatum***
7b. Attack often targets spinal cord and brain; produces brain inflammation known as meningitis	***Cryptococcus neoformans***
8a. Organism is a protozoan	9
8b. Organism is a bacterium	10
9a. Produces chronic diarrhea	***Cryptosporidium muris***
9b. Produces brain abscesses; pathogen sometimes transmitted by domestic cat	***Toxoplasma gondii***
10a. Produces wasting syndrome, anorexia, night sweats, and diarrhea	***Mycobacterium avium intracellulare*** (MAI)
10b. Although it infects people with healthy immune systems, it is more likely to affect the lungs of AIDS patients	***Mycobacterium*** **tuberculosis**

Part B: Other Effects

Not all of the damage associated with HIV infection is caused by opportunistic infections. Some the destruction may result from the immune system's loss of ability to "police" wayward cells. Other damage may be produced by harmful chemicals released by viruses or infected cells.

HIV and Cancer

When a cell becomes cancerous, the chemistry of its surface membrane changes. Immune cells detect and target the "abnormal" membrane. A swift response ensures that the wayward cell will be destroyed before it can produce a clone of tumor-forming offspring.

In the later stages of HIV infection, the ability to destroy cancer cells declines. Tumors appear. Most often these tumors arise in the lymph nodes. Unlike classic **lymphomas**, these AIDS-related tumors spread throughout the body. They can be found in the brain, bones, and heart.

Kaposi's sarcoma has been associated with AIDS since the beginning of the epidemic. This association, however, is changing. At first, physicians believed that Kaposi's sarcoma was a symptom of the infection. Now, scientists think that Kaposi's sarcoma may be caused by a separate, sexually transmitted virus. Under a healthy T_H population, the virus is kept under control. When, the T_H cell count falls, the virus-induced cancer is expressed.

HIV and the Brain

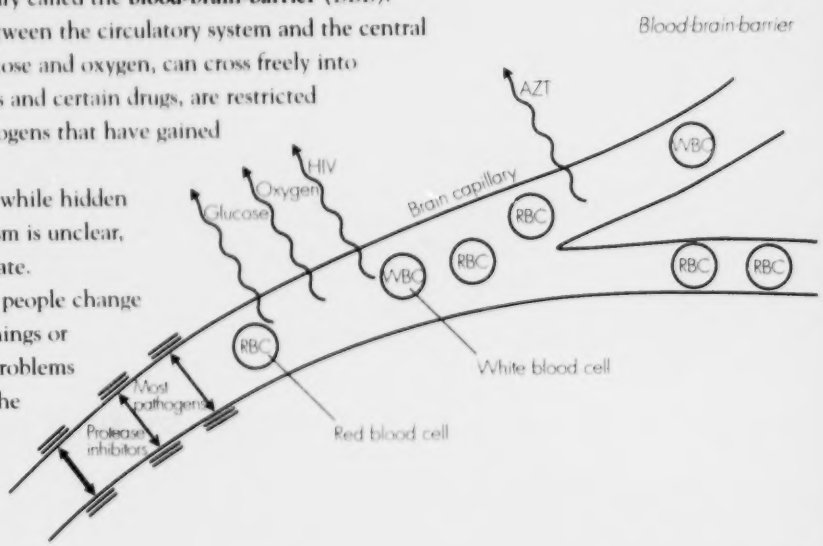
In order for the brain to remain healthy, it must be provided with a constant supply of glucose and oxygen. To meet this demand, brain tissue is nourished by an extensive capillary network.

Brain capillaries are the most densely packed vessels in the body. Unlike other capillaries, they do not let many substances pass through their walls. The cells of capillaries are joined very tightly which produces a physical boundary called the **blood-brain-barrier** (BBB).

The BBB restricts the flow of materials between the circulatory system and the central nervous system. Some molecules, such as glucose and oxygen, can cross freely into the brain. Other molecules including proteins and certain drugs, are restricted from passage. The barrier also keeps out pathogens that have gained entrance to the blood.

HIV is an exception; it crosses the barrier while hidden within infected cells. Although the mechanism is unclear, HIV begins to destroy the patient's mental state.

In the early stages of HIV infection, some people change in the way they think and act. They forget things or respond more slowly. They sometimes have problems concentrating or using fine motor skills. As the disease progresses, the symptoms worsen. Mood swings and personality changes give rise to headaches and seizures. Eventually, the symptoms may end in coma or death.



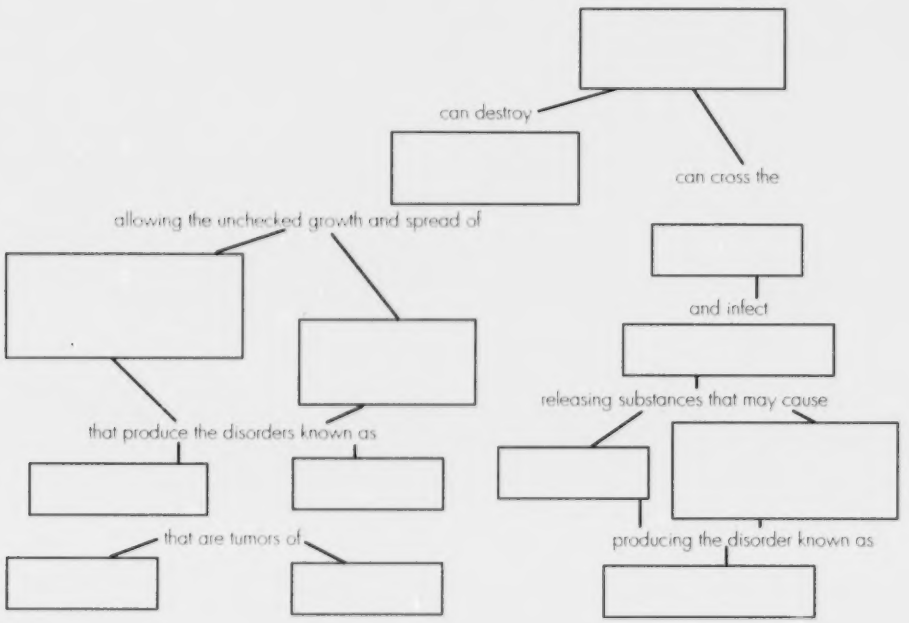
All of the symptoms are lumped together and called **AIDS dementia complex**. Apparently the brain damage is not produced by opportunistic infections. Instead, the brain is injured by the action of HIV.

Some researchers think that this damage comes from HIV's attack on certain brain cells. These brain cells, like macrophages and T_H cells, bear CD4 surface markers. Perhaps the death of these CD4 brain cells severs important connections.

Other researchers believe that AIDS dementia complex is caused by toxic reactions. Perhaps exposure to a viral protein causes a fatal reaction in brain cells. HIV infection may even stimulate the misguided production of chemicals that cause fever, fatigue, and brain cell death.

Questions

Fill in the concept map using words and ideas from the section above.


can destroy
can cross the
allowing the unchecked growth and spread of
and infect
releasing substances that may cause
that produce the disorders known as
that are tumors of
producing the disorder known as

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Symptoms of Infection

Objective

Sudents will use a taxonomic key to identify some opportunistic infections that arise during HIV infection. In Part B, students will read text and answer questions about cancer and AIDS dementia complex, which are other effects of HIV infection.

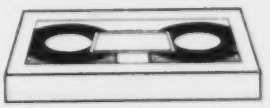
Teacher Notes

Part A: Opportunistic Infections

Display the data below on the chalkboard. Challenge students to represent this information graphically. Suggest using a grid with T_H count as the y-axis and time as the x-axis. Analyze the graph form to explore the relationship between T_H count and opportunistic infections. Remind students that the progression of HIV-related disease and the appearance of opportunistic infections at certain T_H cell counts varies *widely* from person to person.

General Progression of Opportunistic Infections

T_H COUNT	YEARS AFTER INFECTION	OPPORTUNISTIC INFECTION
1000	–	none
800	1	none
600	4	none
400	7	bacterial skin infections
300	7.5	shingles
250	7.8	oral thrush (*Candida albicans*)
200	8.4	*Pneumocystis carinii*
180	8.5	crytosporidium
170	8.6	toxoplasmosis
170	8.6	herpes simplex
50	9.5	cytomegalovirus
40	9.9	*Mycobacterium avium*



Video Connection:
Hear Hydeia (an HIV-positive 12-year-old) describe the various infections she has had over the years. (12:40)

Another young man describes a throat infection which was thrush. (9:08)

The key activity found at the end of the student reading is a unique and active teaching strategy. Instead of reading about pathogens, students actively apply thinking skills to understanding and analyzing the similarities, differences, and features of OIs.

Part B: Other Effects

Review the role of immune system in ridding the body of cancerous cells. Have students apply this understanding to the appearance of AIDS-related cancers. Display a large swatch of netting. Explain that a wrapping made from this fabric will restrict the flow of certain materials. Compare and contrast the wrapping to the tightly packed capillaries forming the BBB. Have students discuss the advantages and disadvantages of the BBB.

AZT, an HIV therapy drug, can cross the BBB; protease inhibitors, another class of drug, cannot. The central nervous system is one of the most difficult body parts to treat for HIV infection.

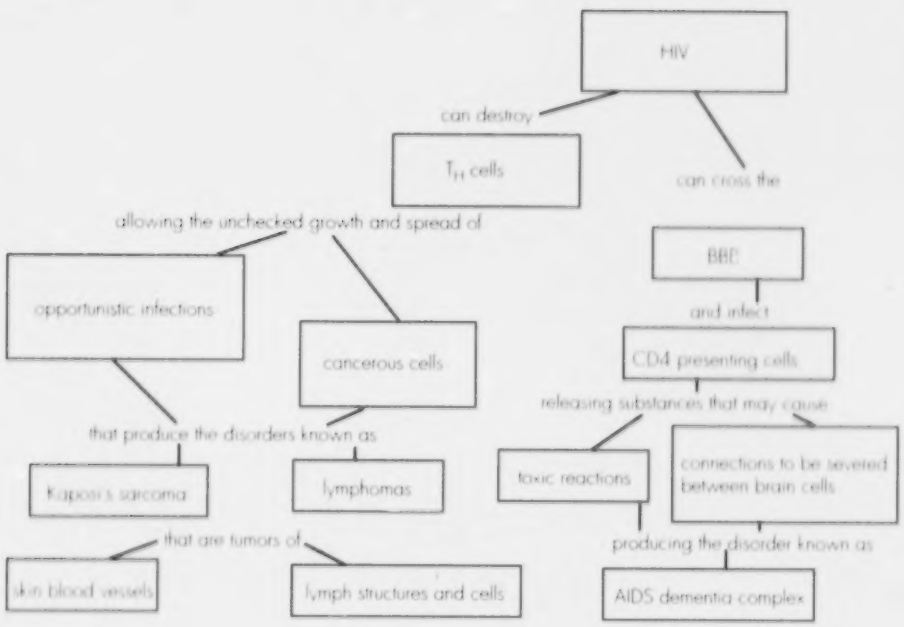
Answers to Student Questions

Part A

1. *Candida albicans*
2. Cytomegalovirus (CMV)
3. *Toxoplasma gondii*
4. *Pneumocystis carinii*
5. *Mycobacterium* tuberculosis

Part B

Concept Map



Vocabulary

AIDS dementia complex - a group of symptoms associated with the declining mental state of some HIV-infected individuals

blood-brain-barrier (BBB) - boundary that restricts the flow of material from the circulatory system to the brain tissue

lymphomas - tumors of the lymph nodes

opportunistic infection (OI) - infection that flourishes in response to growth opportunities

shingles - a skin rash that is produced by the "reawakened" chicken pox virus

TEACHER SUMMARY

CHAPTER FIVE

In the Lab

HIV Diagnostics and Therapeutics

Curriculum Connections

- Viruses
- DNA/RNA Technology
- Laboratory Techniques
- Careers in Science

Chapter Concepts

Chapter Five introduces the concept of how scientists test for, monitor, and treat HIV infection. Researchers are working on three strategies to treat HIV infection: try to keep HIV out of the cell; interfere with the replication of the viral RNA to DNA; and interfere with viral protein manufacture by inhibiting protease action. Advances in medical technology and molecular biology have allowed researchers to develop drugs and techniques which can extend the life of a person infected with HIV, but these do not cure HIV infection. Many of these technologies are still in the experimental stages.

National Science Education Standards

Content Standards 9–12

Content Standard E: Science And Technology

Content Standard F: Science in Personal and Social Perspectives; Personal and Community Health; Science and Technology in Local, National, and Global Challenges

Content Standard G: History and Nature of Science; Historical Perspectives (Molecular Biology; Medical and Health Technology)

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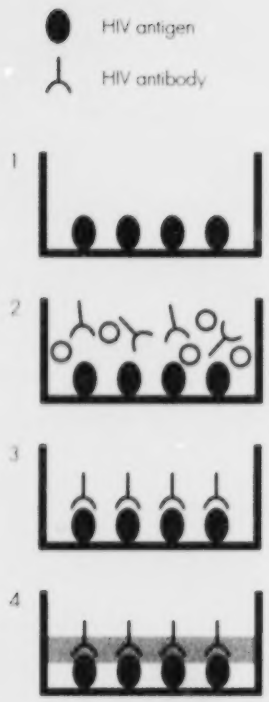
IN THE LAB

Testing for HIV Infection



Can you tell by a person's looks if he or she is infected with HIV? Most likely, not. Outward signs of disease appear only in the most severe stages of infection. The only sure way to verify infection is to test the blood for chemical markers.

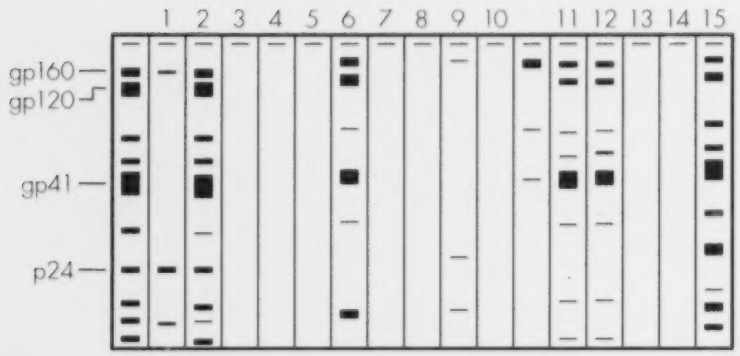
The HIV test offered by most health care facilities and blood banks does not look for virus in the blood. Instead it confirms the presence of HIV by uncovering its telltale antibodies produced by the immune system to fight the virus. In most cases, these proteins become detectable several weeks after exposure to the virus. If HIV antibodies are present in a sample of donated blood, the blood is destroyed. This type of screening helps keep blood supplies safe.

The **ELISA assay** is the most common test for HIV antibodies. Here's how ELISA works:

1. The testing chamber is coated with a layer of HIV-specific proteins.
2. A prepared blood sample is added to the container. If the blood sample contains HIV antibodies, a reaction occurs. The free-floating antibodies bind to the coat of HIV proteins. If no antibodies are present, no binding occurs.
3. The blood sample is washed away. The antigen coat, with any specifically binding antibodies, remains.
4. The chamber is treated with a chemical stain that reacts to antibodies. If antibodies are present, the indicator will change color.

Suppose a person tests positive with the ELISA assay. What is the next step? In most cases, the ELISA assay is followed by a confirmatory test, called the **Western blot assay**.

The increased reliability of the Western Blot test is achieved through a more complex testing procedure. To prepare the Western Blot test strip, HIV proteins are obtained from laboratory cultures of virus. These proteins are separated into distinct bands by a laboratory technique called **gel electrophoresis**. Next, the protein bands are "blotted" onto a test strip.



Western blot strips

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The test strips are placed in contact with blood serum. HIV antibodies present in the blood will bind to specific bands. The strips are washed and then treated with chemical indicators. Like the ELISA test, the presence of antibodies is confirmed by a visible reaction. Since the Western Blot bands contain separate proteins, this test gives a more accurate confirmation of the infection.

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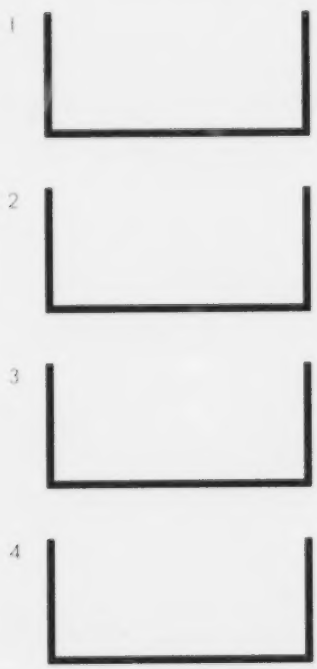
ELISA tray

Questions

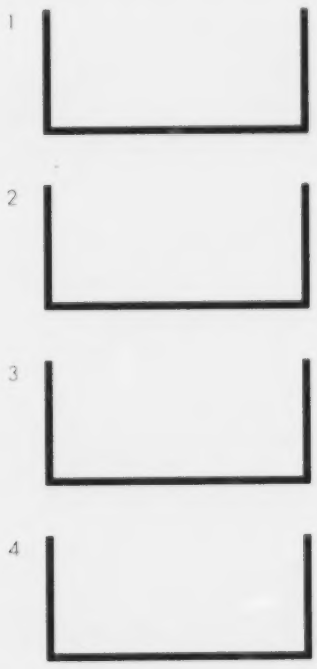
1. Compare and contrast the ELISA and Western blot assays for HIV infection. How are they similar? How are they different?

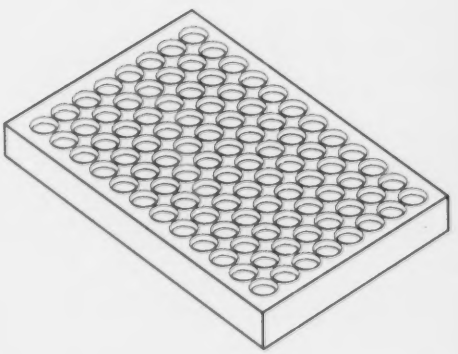
2. Use the diagrams below to sketch the sequence of events that illustrate: (a) a positive ELISA test; (b) a negative ELISA test.

Positive ELISA



Negative ELISA





Testing for HIV Infection

Objective

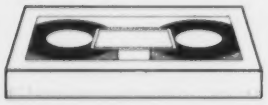
Students read how ELISA and Western blot assays are used to test for HIV infection.

SCREENING BLOOD SUPPLIES: P24 ANTIGEN TEST

When a person is infected with HIV, there is a "window" period of approximately one to two months (it varies among individuals) when tests like ELISA do not detect antibodies to HIV. Obviously, blood banks would like to shorten this period to reduce the chances of accepting donations of HIV-infected blood. HIV antigens (such as the p24 capsid) appear a few days to a few weeks before antibodies to the virus. A test which measures HIV antigens directly could reduce the window period.

Abbott Laboratories developed the first p24 antigen test in 1989, but it was approved only for use in laboratories, not for blood banks. In 1995, the Food and Drug Administration recommended that United States blood banks screen blood for HIV antigens as soon as a test became available. In 1996, two p24 antigen tests were approved for blood bank screening, one from Abbott Laboratories and the other from the Coulter Corporation.

Some studies have shown that p24 antigen tests could detect HIV at about 16–22 days from infection. These tests promise to further reduce the risk (which is slight) of HIV infection by transfusion.



Video Connection:
See ELISA testing equipment and a description of the test procedures. (18:41)

Teacher Notes

Students should understand that most people infected with HIV will not show symptoms for up to several years after infection; nevertheless, the infected person can infect other people.

An ELISA AIDS simutest is an inexpensive module that uses chemically sensitized plates and simulated sera and reactants to demonstrate how ELISA confirms antibody presence. This test can either be performed as a demonstration or a classroom activity. The plates can be reused and the reactants restocked for continual classroom usage.

The AIDS simutest is available through many scientific supply companies. It is produced by Kemtec Educational Corporation, 9889 Crescent Park Drive, West Chester, OH 45069; (513) 777-3535.

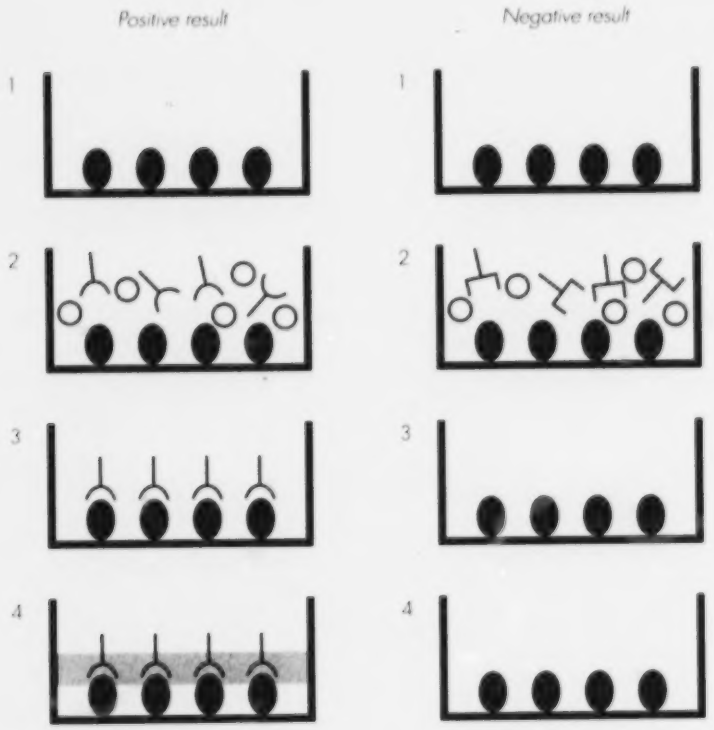
ELISA Uncertainties

Although the ELISA assay is more than 99.9 percent accurate, it does have certain drawbacks.

1. HIV is constantly mutating. New strains may have different surface antigens. The antibodies developed to these strains may not be the complements of the antigens used in testing.
2. The ELISA test is not 100% reliable. Although the frequency of a false reading is less than one in one thousand (0.1%), the wrong results can be devastating to the person who receives the news. To insure the reliability of a positive diagnosis, a confirmatory Western blot is administered when the ELISA test is positive.
3. In a few rare cases, HIV antibodies can take up to several months to appear. A newly infected person may harbor the virus, but test negative for HIV antibodies. Even with negative results, however, he or she can infect others.

Answers to Student Questions

1. Both tests confirm presence of HIV antibodies. ELISA uses a mixture of antigens. Western blot uses specific antigen bands.
2.



Vocabulary

ELISA assay - a basic laboratory test used to test for the presence of HIV antibodies in infected blood

gel electrophoresis - a laboratory technique used to separate a mixture based upon behavior within an electric field

Western blot assay - an advanced laboratory test that can confirm HIV antibodies present in infected blood

IN THE LAB

Monitoring HIV Infection

Like detectives, medical researchers search for clues as to the cause and prognosis of a disease. The clues they are looking for, however, are much less obvious than fingerprints. Mostly, the investigation focuses on the microscopic and chemical indicators of an unseen battle. Researchers construct the progression of disease using cell counts, protein concentrations, and nucleic acid levels.

Measure Numbers of T_H cells

The number of T_H cells reveals how the HIV infection has affected the population of these susceptible immune cells. Healthy individuals have about 1000 T_H cells per ml of blood. Throughout the years of HIV infection, the T_H cell count drops. By monitoring this decline, physicians can roughly monitor the progression of the disease. Armed with this information, they can prescribe more timely and preventative drug therapies.

Measure Antigens or Antibodies to HIV

At a subcellular level, an assortment of antigens and antibodies offers additional clues. Structural proteins of HIV (antigens) are used as clinical markers, including the core protein p24, and the envelope proteins, gp41 and gp120.

The appearance of viral antigens stimulate the production of antibodies. In the first three to four weeks, levels of antigens and antibodies are too low to be confirmed by a laboratory assay. As the amount of HIV in the body (or **viral load**) increases, however, the antigens rise to a detectable level. A few weeks later, the presence of antibodies is confirmed.

Measure Amount of HIV RNA

Researchers also can measure the amount of viral RNA in the bloodstream. The greater the amount of HIV RNA, the larger the viral load. People infected with HIV can have as many as one million HIV particles per ml of blood. Even so, because viruses are so small the total amount of the viral nucleic acid is so slight that it cannot be detected without some sort of chemical amplification.

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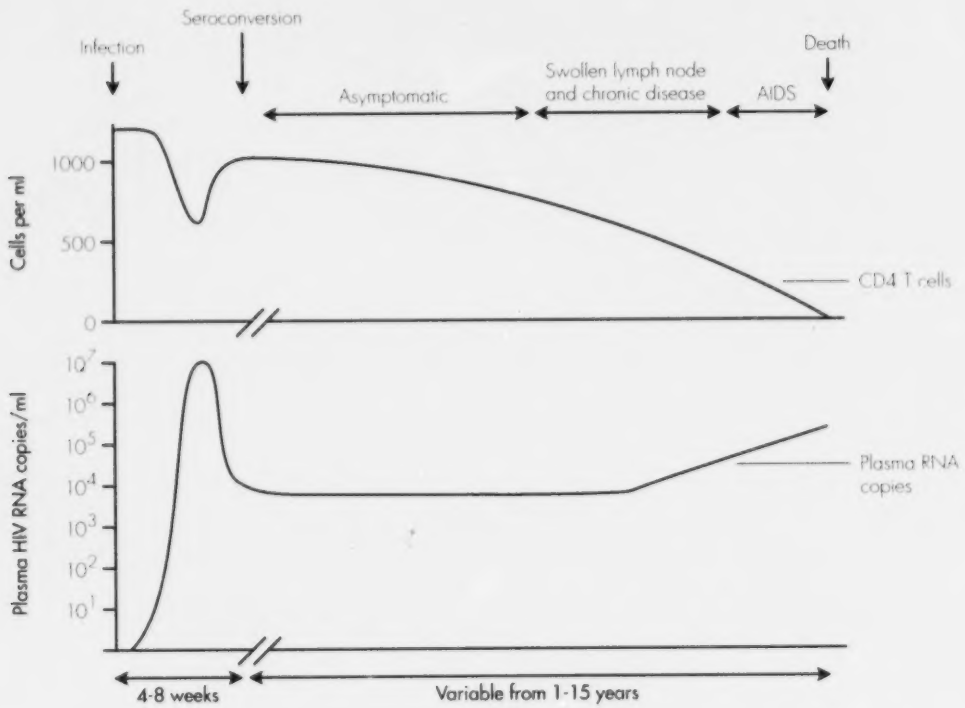
The **polymerase chain reaction**, or PCR, is a laboratory technique that increases the concentration of HIV RNA to a detectable level. To measure the concentration of HIV, a sample of blood is treated and mixed with chemicals that bind to sequences unique to HIV RNA. This binding produces an increased and measurable volume of product.

Increasingly, viral load assays are being used to evaluate new therapies. The viral load can be a better indicator and forecaster of disease progression than the amount of T_H cells.

Examine the blood profiles below. They illustrate some of the clinical markers associated with HIV. Remember that the progression of HIV infection varies from person to person. Not all infections will progress in the same way. Even so, **blood profiles** such as this example can help us understand more about the disease.



Questions

1. What does the double slash on the x-axis represent?

2. Describe what happens to the T_H cell count during the progression of HIV-related disease.

3. Describe what happens to the number of viruses detectable in the plasma as the infection progresses.

Monitoring HIV Infection

Objective

Students will read and interpret a graph of how viral load, cell counts, and antigen markers are used to assess the progression of HIV infection.

Teacher Notes

Discuss how scientists are working hard to find treatments for HIV infection. In order to evaluate therapies, scientists depend upon various clinical markers including viral load and T_H cell counts.

To demonstrate how T_H cells are quantified, prepare a sheet of tag board with fist-size sketches of white blood cells. Color most of the white blood cells with regular poster paint. Color several "marked" CD4 cells with paint that glows when illuminated with a blacklite. In a dimmed classroom, expose the poster to UV illumination. Explain how this technique allows technicians to distinguish and count CD4 cells that have been marked with a flores-cent dye. Use this experience to introduce clinical markers.

To discuss measuring antigens, see margin box on page 130 for a description of p24 antigen tests. This test is used to screen blood at blood banks, but it can also be used to monitor viral load.

Answers to Student Questions

1. A change in the size of the scale. Much happens in the first weeks after HIV infection, so a small time period is expanded to show detail.
2. It falls dramatically several weeks after infection. Although the count rises, it does not regain its original concentration. It enters into a steady and gradual decline.
3. Within several weeks of the initial infection, the plasma viral load rises to its greatest concentration. It then falls and levels off for most of the infection period. Eventually, the levels rise steadily until the patient dies.

Vocabulary

polymerase chain reaction - a laboratory technique that amplifies the concentration of HIV RNA to a measurable level

viral load - the amount of HIV RNA in the body

blood profile - change in blood markers over time

Treating HIV Infection

IN THE LAB

Suppose you have termites infecting a building. For years, this termite population has been devouring the building's wooden frame. You want to preserve and restore the building. In order to do this, you need to address two different, but related problems: (a) get rid of the termites, and (b) repair the damage they have done.

In a similar way, physicians treating HIV infection must also deal with two separate challenges. Doctors must keep the virus at bay and repair and limit the damage caused by opportunistic infections.

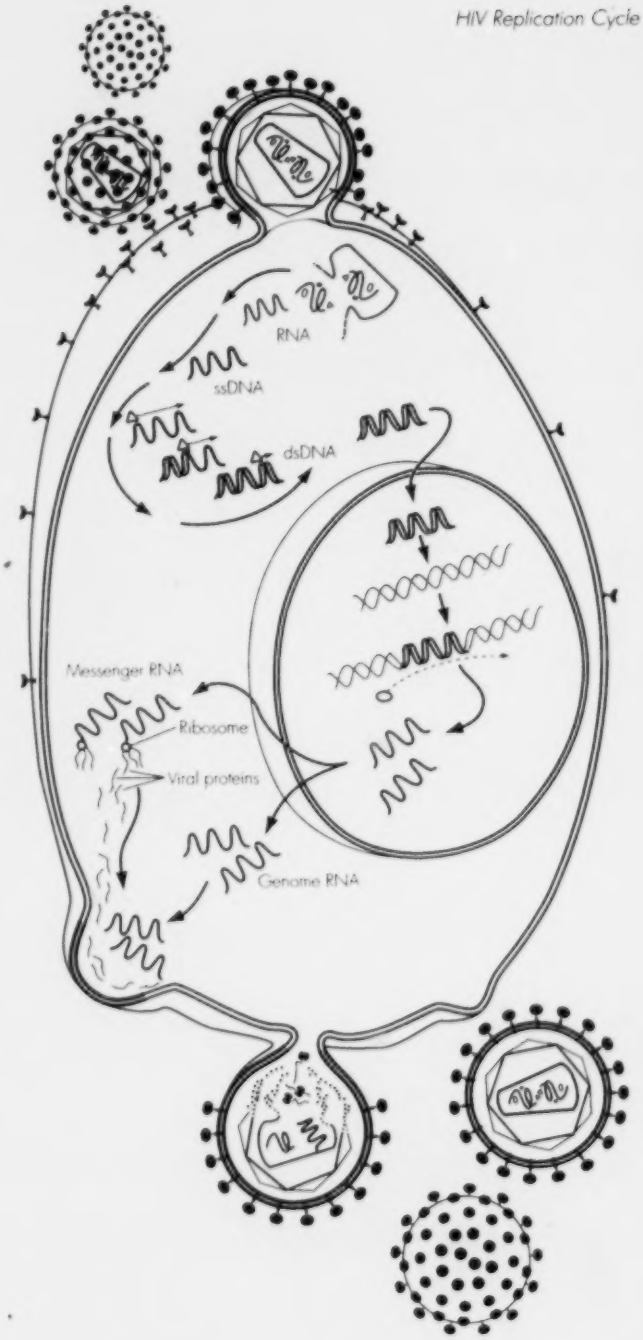
To treat opportunistic infections, physicians use a wide range of antibiotics and antiviral drugs. Some of the drugs target the various infectious organisms. Others are aimed at reducing the symptoms of specific diseases. Boosting the immune system is another tactic used against opportunistic infections. By supercharging the blood with extra antibodies, more pathogens are targeted.

How do you get rid of HIV?

Suppose you were in charge of developing strategies to keep HIV already in the body from infecting new cells. How would you target the virus? Are there particular stages of the HIV replication cycle that are most vulnerable? What types of substances might affect HIV while leaving infected or surrounding cells untouched?

Examine the diagram of the HIV replication cycle. Use it to refresh your understanding of how this virus operates. From what you know about HIV, describe two different strategies that you would pursue to halt the progress of infection. Try to be as specific as possible and try not to damage host cells.

HIV Replication Cycle



Strategy A: Keeping HIV Out

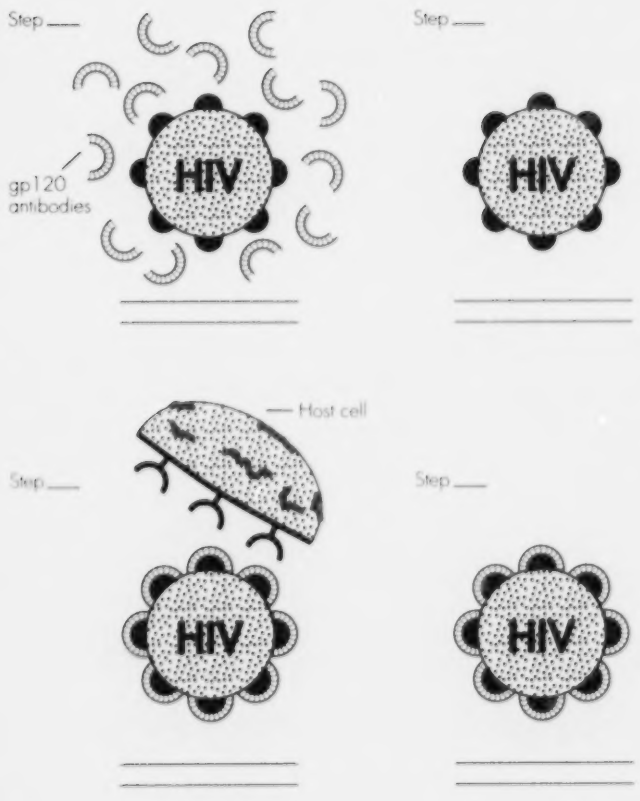
Was one of your strategies based upon keeping HIV out of its host cell? No one has perfected a method to keep HIV out of a host cell, but scientists are working on the problem.

The entrance of HIV into the cell depends upon the binding between the viral protein gp120 and host cell receptors (CD4 and others). By obstructing these sites, the coupling is prevented. If the sites don't bind, HIV can't get in. Some people have genetically abnormal T_H cells which lack the secondary receptor that helps HIV enter the cell. These people seem to be resistant to HIV infection; scientists are studying these abnormal cells to see how they work.

Some other cells that are being studied are taken from **long-term HIV survivors**. These patients have been infected more than 10 years, but do not show symptoms of HIV disease. Apparently, their body has the ability to keep the viral load at a manageable level. By better understanding the action of successful immune systems, researchers may be able to manufacture or stimulate the production of a more effective defense mechanism.

Researchers are also experimenting with free-floating CD4 receptors (soluble CD4 receptors). These receptors are produced through genetic engineering. In theory, the CD4 receptors would act like the surface CD4 sites of immune cells. An HIV particle that contacted the free-floating CD4 receptors would have its binding sites occupied and would be "taken out of circulation."

Researchers are also working on using free-floating CD4 molecules as delivery systems. The genetically manufactured receptors are chemically combined with molecules of toxin. The idea is that when the CD4 receptor binds to an HIV, its poisonous load would destroy or inactivate the virus.



Questions

Examine the diagrams of a cell protection method. Number the sequence in most logical order; then, describe the event that occurs in each illustration.

Strategy B: Interfering with Nucleic Acids

Did your tactics also take aim at nucleic acids? Researchers are aware of the critical role and fragility of nucleic acids. These two features make DNA and RNA primary targets for drug therapy.

DNA Therapy: Understanding the Action of AZT

Zidovudine, better known as **AZT**, destroys the ability of HIV to make viral DNA from RNA. AZT is an impersonator that looks like the DNA nucleotide with thymine, but the likeness is flawed. One end of the AZT molecule lacks the phosphate group needed to continue a DNA chain. When AZT becomes incorporated into a DNA sequence, it prematurely ends the strand. The incomplete segment of viral DNA is useless.

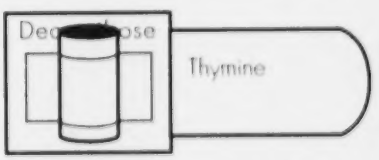
The reverse transcriptase of HIV, which doesn't exist in human cells, is particularly susceptible to the effects of AZT. However, as an imitator of DNA synthesis, AZT, like some cancer chemotherapy drugs, can have serious side effects on the patient's own cellular replication.

Materials

several DNA nucleotide models
heavy stock paper
straw section
tape
scissors

Steps

1. Copy the thymine and deoxyribose sugar outline onto heavy stock paper.
2. Use scissors to cut out both shapes.
3. Tape a section of straw to the middle of the sugar model.
4. Tape the thymine and sugar together. This model represents AZT.
5. Assemble a chain of several nucleotides.
6. Add AZT to the chain.



Model of AZT

Questions

1. How does the addition of AZT affect the replication of the DNA chain?

2. Compare and contrast AZT with the nucleotide thymine. How are they similar? How are they different?

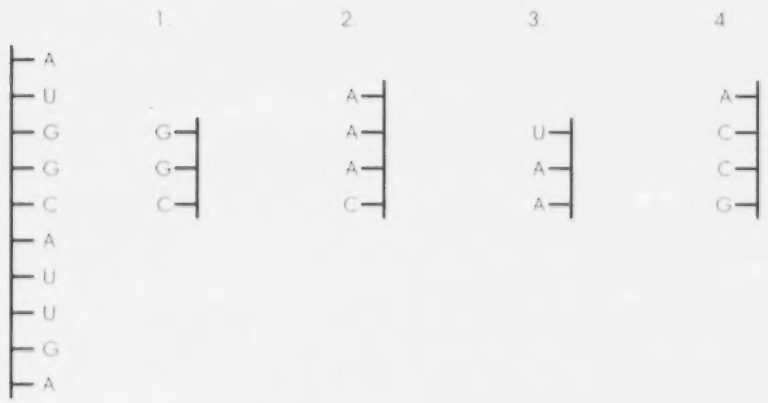
RNA Therapy: Antisense Compounds

A new class of drugs, called **antisense compounds**, disables viral RNA strands. These chemicals target viral code found in the cytoplasm.

Antisense compounds consist of nucleic acid segments. Each free-floating segment contains a short sequence of RNA building blocks. This sequence is the complement to a section of viral RNA. When an antisense sequence encounters its viral RNA complement, the segments bind. This attachment produces a "chemical kink." The kink prevents the entire length of RNA from being read. Without the complete sequence, the viral RNA is useless.

Questions

Which of the numbered RNA sequences can act as an antisense compound to the longer strand on the left? Remember the pairing for RNA nucleotides: A and U go together; C and G go together.



Strategy C: Interfering with Protein Manufacture

Did your strategy target the production of proteins needed to construct new virus particles? If so, then you picked a tactic that many researchers believe is one of the most promising therapies against HIV.

As it comes off the ribosome assembly line, the viral amino acid strand, called a polypeptide, is a raw material. It must be cut into smaller, functional protein units. Some of these units will be assembled into the viral shell. Others will become enzymes essential for retroviral replication.

The enzymes that cut the protein chains at specific sites are called **proteases**. Two different protease enzymes are used to manufacture HIV. One of these enzymes is cellular protease. Cellular protease occurs naturally in healthy cells.

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Protease inhibitor pills

During viral replication, cellular protease is "hijacked" to cut HIV proteins. It acts upon the polyprotein made from the ENV gene. This polyprotein chain contains the amino acid sequences for both gp120 and gp41. Without the action of cellular protease, these viral envelope proteins could not be produced.

The replication of virus also requires the action of viral protease. This virus-encoded enzyme, known as HIV aspartyl protease, is unique to virus replication. It chops the products from both the POL and GAG genes into functional proteins. These proteins include both structural units of the protein shell and the three enzymes carried by the virus.

Since HIV aspartyl protease is found only in cells that harbor HIV, this enzyme becomes a logical target for drug therapy. A class of drugs called **protease inhibitors** interferes with the action of this enzyme. Without the ability to make functional protein units, the viral replication and infectivity is stopped.

Chopping Sites of Protease

Three chains of viral polyproteins are produced by a host cell's ribosomes during a hypothetical infection. The chains are represented by the abbreviated amino acid sequences shown below.

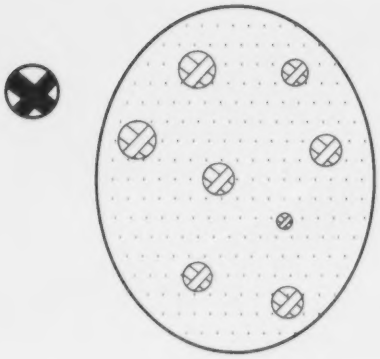
popcornpispnotpapbadpfoodptopeat

appotpofplimapbeanpsoupplastspapwhile

itpispapjobptopseepthepbigpwordsp

All three chains are cleaved by protease enzymes into functional proteins. Analyze the sequences of both the polyproteins and the functional subunits to determine the protease cutting sites.

Treating HIV Infection



Objective

Students read about the current tactics for treating HIV infection. The major point is that none of these therapies "cures" HIV infection and some are only experimental.

Teacher Notes

Hand out page 135 first; after students have given their answers hand out pages 136–139.

Strategy A: Keeping HIV Out

Tape Velcro hook material across the surface of a table tennis ball. Identify the ball as an HIV particle. The Velcro hooks represent the gp120 binding sites. Cut out a large outline of a CD4 cell. Tape small pieces of the complementary Velcro material across the surface of the cell. Identify the material as the CD4 receptors. Challenge students to use these models to develop and illustrate tactics that would prevent the binding between gp120 and CD4. Stress that all tactics to keep HIV out are currently experimental.

Strategy B: Interfering with Nucleic Acids

Have students take out DNA nucleotide models from Chapter One. Use the AZT model to demonstrate how the drug works. An alternative demonstration: supply students with several pop beads that can be used to assemble a plastic necklace. One of the beads should be modified. The nub should be shaved off so that the bead cannot make two connections. Have students use these beads to discuss how AZT interferes with viral replication.

Strategy C: Interfering with Protein Manufacture

Review the steps of protein production. Explain that the amino acid chain that rolls off the ribosome contains several functional proteins bonded together. Use an example of a car transport truck which delivers new cars to the dealers. The whole truck carries several cars, but the individual cars are not useful until they are separated from each other. Have students apply this analogy to the cleaving of polypeptide by protease.

Protease inhibitors are becoming standard therapy for HIV-infected people.

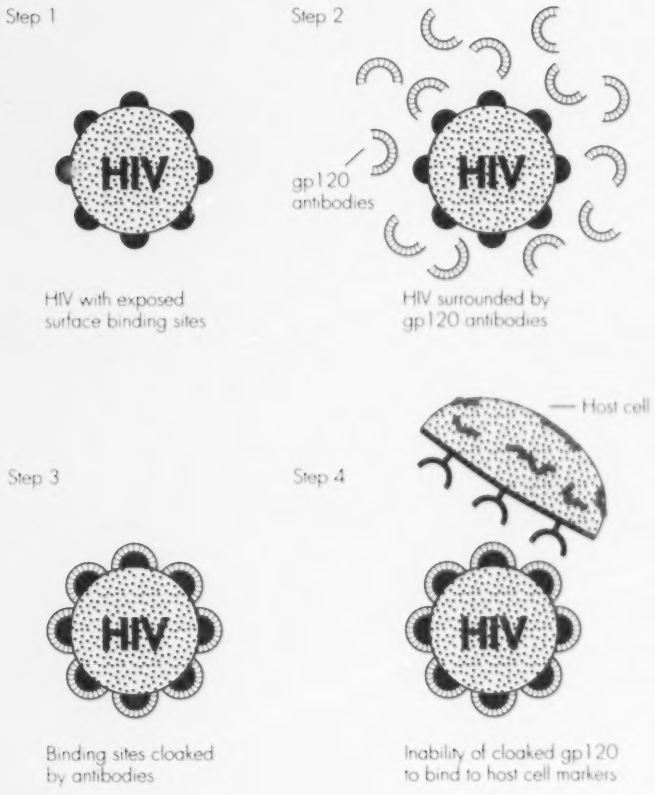
AZT

Although AZT and other nucleoside analogues such as DDC and DDI can impair HIV replication, their effectiveness wears off. Apparently the viral nucleic acid mutates into an analogue-resistant code. The mutation-prone replication cycle may limit AZT's effective period to about one year. Despite this limit, AZT has several important benefits:

- The use of AZT by people with T_H counts between 200 and 500 can delay the progression to AIDS. AIDS patients on AZT therapy may live up to one year longer than expected.
- The use of AZT during pregnancy can decrease the chance of an HIV-infected mother giving birth to an HIV-infected baby.
- The use of AZT reduces AIDS-related dementia. Unlike other antiviral drugs, AZT is effective in crossing the blood-brain-barrier (see page 121).

Answers to Student Questions

Strategy A: Keeping HIV Out



PROTEASE INHIBITORS

Protease inhibitors are the most potent anti-HIV drugs to date. The FDA has approved three brands of protease inhibitors: Abbott Laboratories' ritonavir (or Norvir), Hoffman-La Roche's saquinavir (or Invirase), and Merck's indinavir (or Crixivan). Other pharmaceutical companies are developing protease inhibitors, but these are not yet available by prescription.

Protease inhibitors have been studied as a single drug therapy and in combination with nucleoside analogues, such as AZT. Several combination therapies have shown encouraging success in reducing viral load and increasing CD4 cell counts. However, like some other drugs, over time HIV strains may become resistant to protease inhibitors. Some people have side effects when taking the drugs. Nevertheless, protease inhibitors have improved and extended the lives of many HIV-positive people.

Strategy B: Interfering with Nucleic Acids

AZT

1. The chain cannot continue enlarging. Since AZT lacks the phosphate connector, this building block terminates the chain.
2. AZT contains thymine and deoxyribose sugar. The thymine nucleotide contains thymine, deoxyribose sugar, *and* a phosphate group.

Antisense Complements

Strands 3 and 4 can act as antisense compounds as shown.

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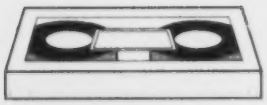
Strategy C: Interfering with Protein Manufacture

The three amino acid chains should be chopped by protease into the following "proteins" (each word is a protein):

popcorn is not a bad food to eat
a pot of lima bean soup lasts a while
it is a job to see the big words

Vocabulary



Video Connection:
See Hydeia and Patricia take medicines to treat HIV infection. (24:15)

Protease inhibitor packaging is also featured. (26:17)

antisense compounds - segments of nucleic acid that are the complements to portions of viral RNA

AZT - a nucleoside analogue that replaces thymidine in DNA synthesis

long-term HIV survivor - a person who has survived many years of HIV infection with few, if any symptoms

protease - an enzyme that cleaves polypeptides into functional proteins

protease inhibitor - a chemical that inhibits the action of protease

Zidovudine - another name for AZT

HIV Vaccines

HIV infection is a continual and deadly battle. Cell death is accompanied by the destruction of millions of viral particles. Like many global conflicts, this is a war of attrition. Both sides lose. However, the viral particles replenish their armies at a much quicker rate. Eventually, the sustained supply of HIV outweighs the dwindling defenses. The immune system collapses.

Let's backtrack. For a moment, suppose that the war never got to this level. In its earliest stage, HIV infection was prevented from establishing a foothold. If that were the case, the immune system would not become overwhelmed. Instead, the defenses would destroy the viral intruders without suffering serious damage. This type of early response is produced by vaccinations.

HIV Vaccines

Researchers are working on the development of two types of HIV/AIDS vaccinations. One type of vaccination is aimed at preventing HIV from ever establishing itself in the body. Like a polio vaccination, this therapy would prime your immune system to deal with a first-time HIV infection. A second type of vaccine would help those people already infected with HIV. Like the rabies vaccine, this vaccine would stop the progression of symptoms. HIV-infected people would still have the virus, but they would not progress to the life-threatening symptoms of AIDS.

Types of Vaccines

All vaccines walk a "chemical tight rope." In order to produce a protective immune response, a vaccine must be similar enough to the disease agent so that the immune system reacts as if reacting to the agent itself; but the vaccine must not be so similar as to produce disease symptoms. There are several types of vaccines used to to produce viral immunity.

Attenuated virus vaccines are weakened forms of the actual disease-causing agent, and they produce few, if any, disease symptoms. When introduced into a person, these viruses establish a long-lasting infection. This infection does not cause illness. Instead, the infection prepares the immune system for an encounter with the disease causing virus. A good example of this type of vaccine is the Sabin version of polio vaccine.

Inactivated virus vaccines are preparations of the actual disease-causing agent that have been destroyed by chemicals or radiation. When this type of vaccine is given, it too will trigger the immune response, but in many cases the response is temporary. Unlike the attentuated viruses that establish a "foothold" in the host, these particles are removed from the body by the immune system. To insure a lasting immunity, they often must be reintroduced with a series of booster shots. A good example of this type of vaccine is the Salk version of the polio vaccine.

Both of these types of vaccines have been widely used to immunize the population against a variety of diseases. But one concern with these vaccines is safety. Occasionally an attentuated virus can mutate back into a disease-causing form, and when inactivating virus it is not always possible to insure that all viruses in that preparation have been inactivated.

With the advent of genetic engineering, vaccines are now being made that closely resemble the disease agent but are much safer than attenuated or inactivated vaccines.

The **virus protein vaccine** is one such type. Through genetic engineering, one or several of the virus proteins or pieces of protein are made, and when introduced into the host these vaccines induce an immune response. When the infectious pathogen appears, bearing the proteins present in the vaccine, the pathogen is targeted by the immune system and destroyed. Another way of exposing the immune system to virus proteins is to introduce single virus genes in the form of a **DNA vaccine**. The DNA in the vaccine actually gets taken up by the host's cells, the cells produce that single virus protein and the immune system responds. Finally, the same virus gene can be introduced into the genome of an unrelated, non-disease-causing organism, and that organism can be introduced into the host as a **live vectored vaccine**. Again, the host will produce the protein from the pathogen and the immune system will be primed for a response to the real pathogen.

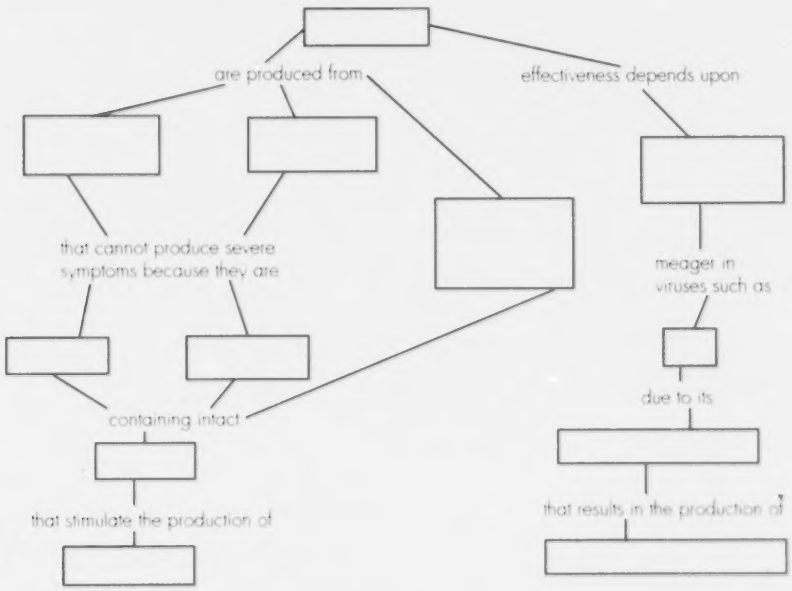
Hitting the Moving Target

The effectiveness of any vaccine depends upon the agent it targets. If an agent produces identical copies of itself, targeting is simplified. Researchers select a common antigen and introduce that as the vaccine. But if the agent has many different appearances, targeting is much more difficult.

HIV replication is highly error-prone. The mutations create strains with differences in their surface proteins. These differences make it difficult to produce a vaccine that can target all strains. Some types of wide-spectrum vaccines against most HIV strains are being tested in laboratories. Researchers hope that a vaccination against HIV can be available in the years to come.

Questions

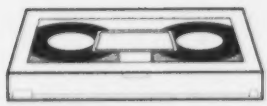
Fill in the concept map using words and ideas from the section above.


are produced from
effectiveness depends upon
that cannot produce severe symptoms because they are
meager in viruses such as
due to its
containing intact
that stimulate the production of
that results in the production of

HIV Vaccines

Objective

Students read about the challenges associated with developing an HIV vaccine.

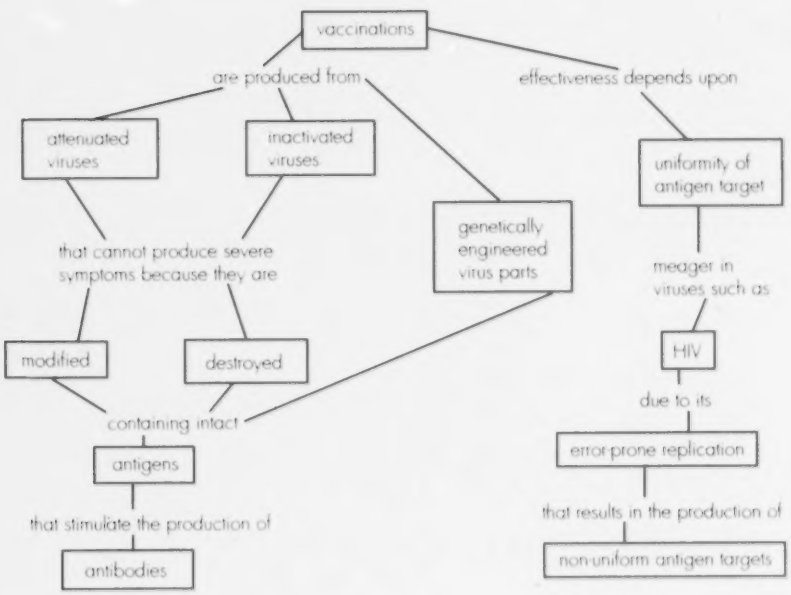


Video Connection:
See discussion of vaccines and animations of DNA and RNA replication.
(22:14)

Teacher Notes

Review the structural components of HIV. Then challenge the students to create a "wanted poster" that describes HIV virus. The poster content should include a description of the virus structures that can be recognized, distinguished, and targeted by immune cells.

Answers to Student Questions



Vocabulary

attenuated virus - the virus replicates, but cannot produce full blown disease symptoms

inactivated virus - a virus that no longer replicates

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TEACHER SUMMARY

CHAPTER SIX

Outside the Lab

Communication and Prevention

Curriculum Connections

- Disease Epidemics: Past and Present
- Human Sexuality
- Personal and Community Health
- Statistics

Chapter Concepts

Chapter Six introduces students to the idea that accurate information about HIV needs to be shared. Scientists share results of research; students should discuss the issue with friends; the media has a role in getting the word out about HIV and AIDS to everyone. As a member of society, each student should understand that unfounded fears about HIV lead to discrimination against and sometimes outright cruelty toward HIV-infected people. HIV is not spread through casual contact, and infection can be prevented. Statistics for the AIDS pandemic in the United States and worldwide are offered to give students an idea of the magnitude of the spread of HIV.

National Science Education Standards

Content Standards 9–12

Content Standard A: Understandings About Scientific Inquiry (results of scientific inquiry communicated between scientists)

Content Standard C: Behavioral Biology (links to psychology and sociology)

Content Standard F: Personal and Community Health; Natural and Human-Induced Hazards; Science and Technology in Local, National, and Global Challenges

Outside the Lab

Communication and Prevention

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OUTSIDE THE LAB

Communication

HIV/AIDS stories appear on almost a daily basis in a broad variety of media, including newspapers, journals, radio, and television. This wasn't always the case. In the early 1980s, little was written about the mysterious national epidemic. By the middle of the decade, the media reached a turning point.

As informed citizens, it's important to keep an eye on how the media covers such a crucial health issue. How much information do you think the media gives about important HIV/AIDS discoveries? In a world where the average sound bite lasts for a brief seven seconds, do you think important facts get lost in a whirlwind of competing messages?

If you think the media could be doing a better job, try to identify how they might do that. Is the problem lack of coverage or quality of coverage? Also, give some thought to how well the public "hears" that information. Because communication is a two-way process, the media must be able to tailor their coverage so that we, their audience, understand the news.

In this activity you will look at reporting HIV/AIDS from both the media's and the public's perspective. First, take a few minutes to think of the last time you saw or heard a news story on HIV/AIDS. On a blank sheet of paper, list all the facts you remember from that broadcast. How much information did you retain? Try explaining the story to a partner. Did you have enough facts to relate the whole story? Between you and your partner, list several ways the media can report HIV/AIDS so that their coverage will be meaningful and important to their audience.

Now, use your list to write an actual news story. Pretend you and your partner are the editors of a radio news show. Use a newspaper story on a recent HIV/AIDS development. If you have a one-minute broadcast, the most time you can spend on this story is 30 seconds. Write a 30-second radio spot based on the newspaper clipping. Be sure the first sentence of your story is interesting. Journalists call this sentence the lead, and they use it to grab the listener's attention. Read your radio spot aloud to each other, changing your words and the amount of information you give to fit your 30-second time slot.

When you are happy with the way your story sounds, trim it again so that it fills a 10-second time slot. What do you cut? How do you decide?

HIV INFORMATION ON THE INTERNET

The Internet offers many resources for "downloading" information about HIV/AIDS. You can learn about the latest therapies, new research, and sources of help. There are even **chat rooms** in which people can share their thoughts about HIV disease. If you navigate to the right places on the Internet, you can access research results from on-line scientists. Before this type of communication was available, scientists had to read about research results in scientific periodicals. Although printed journals are still a primary source of information, and an archive method for research, many scientists keep up with research news by going on-line.

Questions

1. What medium (newspapers, news from the Internet, radio, television, etc.) do you think is the best way to get information about HIV/AIDS? Why?

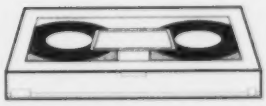
2. Does the general public get exposed to important information about HIV/AIDS research?

3. Who should educate the public on recent HIV/AIDS developments? Should it be the government, the media, researchers, the public itself? Explain your answer.

Communication

Objective

Students design some methods for communicating scientific information about HIV and AIDS to understand why reporting on the subject can vary in quality.



Video Connection:
Use the video as an example of ways to communicate information about HIV.

Teacher Notes

Discuss the role of communication. Have students compare and contrast different media. This book and the video are examples of communicating about HIV. As they go through the development stages of their radio spots, encourage students to notice how the time limits the content. What does this tell them about the kind of information they can learn best from various media? Explain that research information is mostly shared through scientific journals.

The Library and Scientific Journals

You may wish to display some of the original journal articles that described the early years of the epidemic before the causative agent (HIV) was identified and isolated. Most can be located in local hospital libraries. These citations include:

1. Centers For Disease Control and Prevention. "Kaposi's Sarcoma and Pneumocystis Pneumonia among Homosexual Men—New York City and California." *MMWR* 30 (1981): 305–308.
2. Centers for Disease Control and Prevention. "Epidemiological Aspects of the Current Outbreak of Kaposi's Sarcoma and Opportunistic Infections." *N Engl J Med* 306 (1982): 248–252.
3. Ammann, A. J., Cowan, M. J., Wara, D.W., et al. "Acquired Immunodeficiency in an Infant: Possible Transmission by means of Blood Products." *Lancet* 1 (1983): 956–958.
4. Small, C. B., Klein, R. S., Friedland, G. H., et al. "Community-Acquired Opportunistic Infections and Defective Cellular Immunity in Heterosexual Drug Abusers and Homosexual Men." *Am J Med* 74 (1983): 433–441.
5. Elliott, J. L., Hoppes, W. L., Platt, M. S., et al. "The Acquired Immunodeficiency Syndrome and Mycobacterium Avium-Intracellulare Bacterium in a Patient with Hemophilia." *Ann Intern Med* 98 (1983): 290–293.

Internet Information

There is a wealth of information available on the Internet. If students have access to a World Wide Web connection, encourage them to research information for their radio spots, to download images for their video spots, or to research answers to any of their questions on *The Science of HIV* through the Internet. See pages 170 and 171 for a suggested list of Internet sites.

The Media

You may also wish to have students brainstorm about why they think the media increased their coverage of HIV/AIDS. Students might wish to call journalists at a local paper and

"interview" them about this question. They could also do library or Internet research to see when coverage began to increase, and whether that increase was sparked by a particular person or event. For example, well-known people such as Ryan White, Greg Louganis, Magic Johnson, and Arthur Ashe have contributed to HIV/AIDS coverage in the mainstream media.

Tabloids and Newspapers

Show students some examples of tabloid papers. Then, show them examples of reporting on HIV from a respected large circulation newspaper (i.e., *The New York Times*, *Washington Post*, *Los Angeles Times*). Have students discuss how tabloids can sometimes contain incorrect or misleading information about HIV. Ask students how that affects people who read the tabloids. Tabloids can be more willing to run controversial stories. Have students discuss whether publishing controversial stories is a good or bad way to convey information about HIV.

STORYBOARD ACTIVITY

The video producers who developed the video that accompanies this book began their work with a process called "storyboarding." A storyboard looks like a comic strip. It shows the most important elements of the shot that will be captured by the camera. It also includes the sounds or words that accompany the image.

Have students turn their 30-second news spots into a television news broadcast. They don't actually need a video camera; they can create a simple storyboard for their story. Before they begin, have them decide what pictures—moving or still—would add to the message they want to send. They may need to edit the broadcast to allow the pictures to do some of the story telling. Distribute copies of the blank storyboard cells (page 151) for students to create their final version.

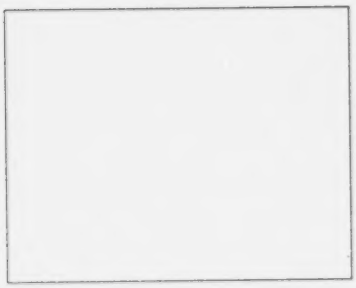
Answers to Student Questions

Content will vary according to student sophistication, knowledge, and creativity. Remind students that they can find a great deal of information through research. In fact, the information in this book was researched in local libraries, through the Internet, and by discussions with scientists working on HIV.

Vocabulary

chat room - area of an on-line service that offers real-time communication

VIDEO

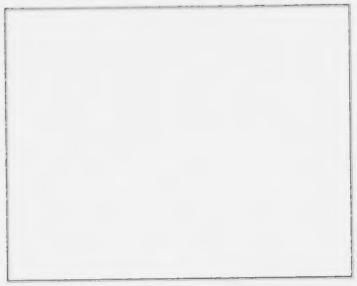


AUDIO

VIDEO

AUDIO

VIDEO



AUDIO

VIDEO

AUDIO

Stopping the Spread of HIV/AIDS

Part A: Improving Your Chances

Ideas can spread faster than viruses. Yet, the epidemic continues to grow. In this year alone, several hundred thousand Americans will become infected with HIV. Most of them will not be aware of their infection. They may pass it on to others *before* they are tested or show symptoms of sickness.

In the United States, the use of infected needles and syringes accounts for some of the spread of HIV. When intravenous (I.V.) drug users share their **works**, they increase the chances of introducing the virus directly into their blood stream.

Worldwide, intimate sexual contact accounts for most of HIV's spread. The only sure way to protect yourself from sexual transmission is to not have sex, including oral sex. If, however, you are sexually active, protect yourself. Consider actions that will reduce the risk of infection.

The risk of becoming infected with HIV is lowered when you:

- reduce the number of sexual encounters;
- engage in sexual acts with fewer partners;
- engage in sexual acts in which there is less contact with infected semen, vaginal secretions, or blood.

Mathematics and Probability

A deck of 52 playing cards is sorted into four piles of thirteen cards. One of the cards is marked.

1. Pick one pile. What are the odds that this pile contains the marked card?
2. Suppose you selected two piles. How would this change your odds? How would picking four piles change your odds?
3. Suppose you selected a pile that contained the marked card. If you were to pick one card from this pile, what are the odds that this card was the marked card?
4. Suppose you were able to pick two cards instead of one. How would this change your odds of picking the marked card? How would picking three cards change your odds?
5. Apply the playing card example to the risk of HIV transfer. How could you represent:
   a. an increase in the number of different partners?
   b. an increase in the number of sexual encounters with the same partner?
6. What type of playing card analogy would represent the increased risk associated with more likely contact with infected fluid from the same partner?

Part B: Barriers

Anyone can become infected during intimate sexual contact with an infected person. It doesn't matter whether you are straight, gay, lesbian, or bisexual. Infected sexual fluids do not discriminate according to sexual orientation. The only *sure* way to protect yourself from sexual transmission is abstinence. If you are sexually active, there are ways of reducing the risk of infection.

A **condom** is an HIV barrier. There are male condoms that fit over the penis and female condoms that are inserted into the vagina. When used correctly, condoms form a barrier that can prevent HIV from being transferred. To ensure the effectiveness of a condom, you should use only ones made from latex. Animal skin condoms are made from material that is more likely to allow the passage of HIV.

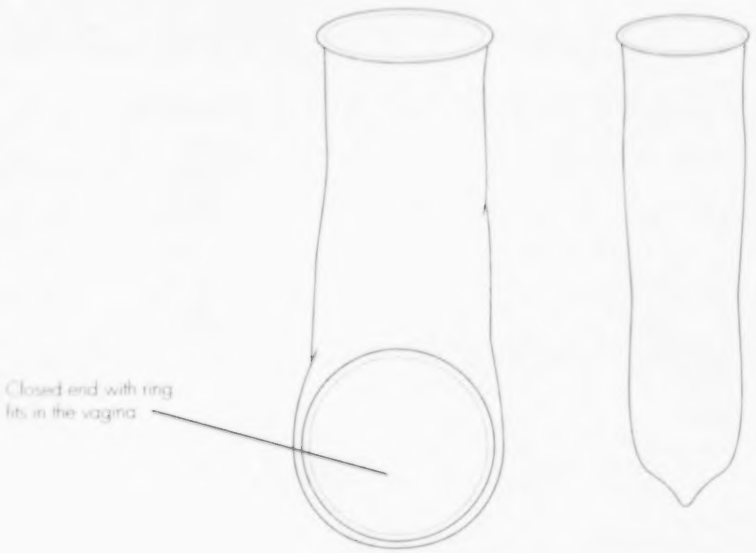
Another type of barrier called an **oral dam** prevents HIV from being transferred through the mouth. Like a condom, this sheath prevents HIV from contacting surfaces that are susceptible to infection.

Condoms and oral dams are purchased over the counter at most drug stores. To insure effectiveness, follow the directions on the package. Many condoms are sold with the spermicide **nonoxynol-9**. Originally developed to destroy sperm, this chemical also will inactivate HIV.

Once the condom or oral dam is in place, it shouldn't be removed until the end of intimate sexual contact. The used barriers must be disposed of properly. No one should come in contact with its surface or contents.

HISTORY OF CONDOMS

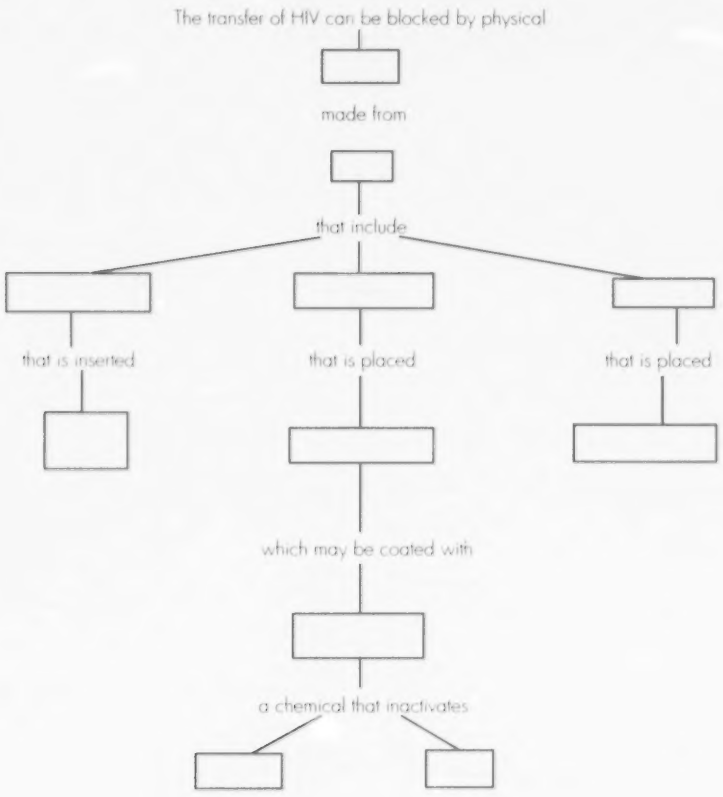
Condoms were first developed in ancient Egypt. Over time, their use spread to other countries and continents. Some historians believe that the condom's widespread use may have controlled the spread of sexually transmitted diseases (STDs). The microbes that cause syphilis and gonorrhea cannot pass through a condom. Likewise, a latex condom halts the spread of HIV.



Female condom *Male condom*

Questions

Fill in the concept map using words and ideas from the section above.



Part C: Clean Needles

Your skin is a tough and resistant barrier. Its dense concentration of cells acts like a physical shield to keep out all sorts of germs and viruses. However, when the skin is broken, the protection is lost.

Sometimes, cuts, tears, and injuries to the skin can't be helped. A break in the barrier creates a two-way route. Pathogens on the outside can get in. At the same time, blood can get out.

Perhaps the surest way to become infected with HIV is to receive HIV-infected blood. Since 1985, donated blood has been screened for HIV. This screening has virtually eliminated the chance of being transfused with HIV-contaminated blood. Likewise, blood products also have been screened insuring that they, too, are HIV free.

Even so, blood transmission remains the major route of HIV infection in the United States. Instead of being transferred during medical procedures and treatments, the virus is now spread mostly by infected needles and syringes.

Intravenous (I.V.) drug users use needles and syringes to inject drugs into their bloodstream. Often these devices are shared among users. As they are passed from one person to another, droplets of blood remain in the **works**. If some of these droplets contain HIV, the virus may infect the next user.

To prevent the spread of HIV, never share needles. This includes needles that are used for piercing, tattoos, electrolysis, and acupuncture. Even for body piercing, make sure that the needle is sterile. Disposable needles are your best bet against infection. If disposable items are not available, you can get some protection by washing the needles and syringes in bleach.

In addition to sharing needles, smoking from the same crack cocaine pipe can also increase the risk of infection. Some crack pipes are made of materials that heat up quickly. The high temperatures can burn sensitive lip tissue. This tissue can blister, crack, and form open sores. As a pipe is passed from user to user, it can become contaminated with HIV-infected blood. HIV can enter through open cuts or lip sores.

YOUR OPINION COUNTS!

Should I.V. drug users have access to a public needle exchange program? In many communities across the nation, health agencies offer a free needle exchange program. I.V. drug users exchange their used "works" for sterile needles and syringes. Some people argue that this type of program supports drug abuse. They feel that the I.V. drug addicts are criminals and should not be supported by the community. Others argue that the spread of HIV through sharing of contaminated needles is increasing at an alarming rate. What is your opinion?

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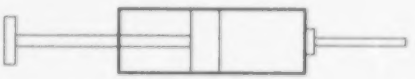
Assessing Risks

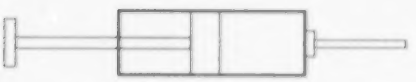
Number the works described below according to how likely they are to be infected with HIV. #1 is most likely to be infected with HIV and #4 least likely to be infected with the virus. Give reasons that support your placement.

Shared, but soaked overnight in bleach



Immediately shared with users of unknown HIV status

Unused, still within sterile packaging



Unused, but not in original sterile packaging

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Stopping the Spread of HIV/AIDS

Objective

The objective of this section is to present an introduction to methods that stop or reduce the spread of HIV.

Teacher Notes

Part A: Improving Your Chances

Display or wear a surgical face mask. Identify the face mask as a barrier that may limit the spread of microbes transferred through casual contact. Explain that masks such as these were worn by civil service workers during the flu pandemic of 1918. During that outbreak, there were more than 500,000 deaths and over 20,000,000 cases of flu reported in the United States.

Discuss the ineffectiveness of face masks against the spread of HIV. Compare and contrast casual and non-casual contact.

Part B: Barriers

Display a latex glove. Identify latex as the material from which condoms are constructed. Fill the glove with water and hold it overhead. Explain that water cannot pass through the molecular structure of latex. Likewise, the latex also restricts the passage of cellular and subcellular particles including sperm, HIV, and the microbes associated with sexually transmitted diseases.

Part C: Clean Needles

Stress to students that any needles that puncture the skin should be sterile. To demonstrate the transfer of HIV through shared needles, you'll need a syringe, a test tube half filled with saturated sodium chloride solution, a test tube half filled with distilled water, and a reagent bottle filled with 0.2M silver nitrate (3.4 grams of silver nitrate in 100 ml of solution). Label the test tube containing the sodium chloride solution "User 1." Label the test tube containing the distilled water, "User 2."

First, fill the syringe from the sodium chloride filled test tube. Return the solution to the test tube. Fill the syringe again and return (as best you can) all of the sodium chloride into a stock beaker. Now, place the syringe in the test tube labeled "User 2." Draw up the water and release it several times. Set the syringe aside.

Add several drops of silver nitrate to this test tube. Display the change in appearance of the contents. Explain that the silver nitrate reacted with the sodium chloride that was left behind within the syringe.

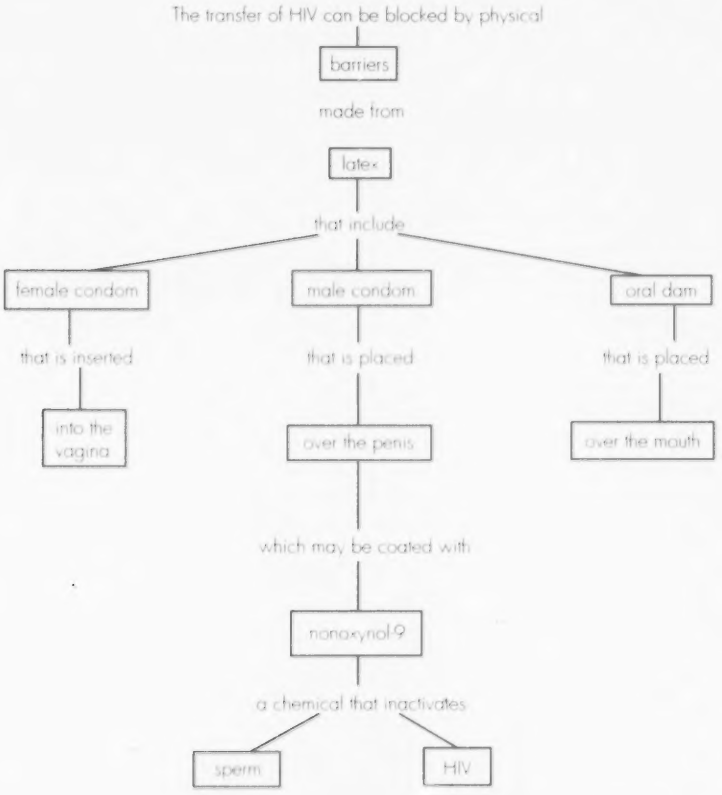
Challenge students to apply this observation to the transfer of HIV by contaminated needles and syringes. How is it similar? How is it different?

Answers to Student Questions

Part A

1. 1 in 4, or 25% probability
2. 2 in 4, or 50% probability; 4 in 4, or 100% probability
3. 1 in 13, or about 8% probability
4. 2 in 13, or about 15% probability; 3 in 13, or about 23% probability
5. a. By increasing the number of piles selected
   b. By increasing the number of cards drawn from a pile
6. Selecting a greater number of cards from a pile at one time

Part B



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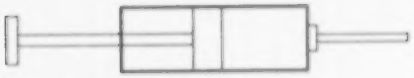
Part C

3



Shared, but soaked overnight in bleach

Although shared, the bleach soaking most likely deactivated HIV viruses that contaminated the syringe

4

Immediately shared with users of unknown HIV status

If the syringe was shared with a HIV infected individual it might harbor an infective dose of virus

1

Unused, still within sterile packaging

Since the package was unopened, this is the only syringe that is most likely sterile

2

Unused, but not in original sterile packaging

Although it was unused, it is no longer sterile. It might harbor other pathogens.

Vocabulary

condom - sheath that covers the penis or is inserted into the vagina

crack - a potent form of cocaine

nonoxynol-9 - a spermicide that is effective in inactivating HIV

oral dam - a piece of latex used to cover the mouth during oral-genital sex

works - slang for needle and syringe

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OUTSIDE THE LAB

Social Issues

Everyone has certain responsibilities. At home, you may have to set the table or wash the dishes. Perhaps, it is your job to care for a pet. Even when these chores are completed, your responsibility isn't over. There's always homework.

But responsibility means more than completing everyday routines. It is a way of dealing with the world in a mature, educated, and unselfish way.

By now, you've learned plenty about HIV and AIDS. This knowledge has probably affected the way you think about HIV disease. Perhaps your views on people who have the virus have changed as well.

Part A: HIV and Prejudice

Many people who have HIV and AIDS face more than health problems. They encounter prejudice. Sometimes, the prejudice may surface as an unkind remark or action. Other times, it can be more destructive. For example, a few years ago, some people burned down the house of an HIV-infected student. Perhaps these people thought that they could catch HIV just by living in the same town as the student.

Think about the different ways HIV prejudice might affect the school, community, and workplace environment. Use your thoughts to complete the chart "HIV and Prejudice."

Part B: HIV and the Law

Legal aspects are seldom clear cut. Even so, many laws have been passed about HIV and AIDS. There are laws that protect the rights of people infected with HIV. There are other laws that protect the rights of people who are uninfected with the virus.

Some laws and rulings apply directly to discrimination. They insure that people infected with HIV will be treated equally and fairly. Others protect the rights of privacy.

Here is your chance to be a law maker. Think about the legal issues that relate to HIV disease. Use the chart "HIV and the Law" to describe four laws. Two of the laws should ensure the rights of people infected with HIV. Two of the laws should ensure the rights of those people who are not infected with HIV.

HIV and Prejudice

Describe three acts of prejudice directed toward someone infected with HIV. Give an example from school, community, and workplace environments.

Act of prejudice	Underlying motive(s)	Misconceptions associated with motive(s)	Effect(s) upon HIV-infected individual	Effect(s) upon the community	How should it be addressed?
1.					
2.					
3.					

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Laws that Protect the Rights of HIV-infected and Uninfected People

Brainstorm all of the legal issues that are associated with HIV infection. From your list, identify four issues that can be addressed by laws and legal action. Two of the laws must ensure the rights of people who are infected with HIV. Two of the laws must ensure the rights of people who are not infected with HIV. Describe all four laws and address the concerns listed in each column.

Description of law	Whose rights will the law ensure? Be specific.	Describe the best way to implement this law.	How will the law be enforced?
1.			
2.			
3.			
4.			

Part C: Personal and Social Responsibility

Consider this: we are approaching the third decade of the AIDS epidemic. There have been many kinds of HIV/AIDS books, television shows, movies, radio broadcasts, concerts, interviews, magazine articles, pamphlets, courses, and talks. Yet, the disease continues to spread.

When it comes to HIV and AIDS, everyone has a responsibility. It doesn't matter whether you practice high-risk behaviors or not. Your responsibility involves sharing knowledge to help other people understand about HIV/AIDS.

Combating ignorance, however, is only the first step. Just learning about the disease is not enough. People must do something with their knowledge. Often, this involves the most difficult challenge of all—changing behaviors.

Social responsibility may not be easy. Neither are the answers to many questions that concern HIV infection and AIDS.

Work with members of a team. Discuss each of the questions or statements presented below. Write down your team's best responses.

1. What are the best ways for an individual to help stop the spread of HIV?

2. What are the best ways for a community to help stop the spread of HIV?

3. What are the best ways to encourage behavior changes?

4. In what ways can someone who does not engage in high-risk behavior become more socially responsible?

5. In what ways can someone who does engage in high-risk behavior become more socially responsible?

6. What are the best ways to educate people about HIV and AIDS?

Social Issues

Objective

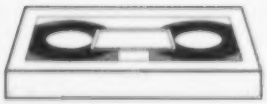
Students develop an overview of the personal and social issues associated with HIV and AIDS.

Teacher Notes

First, use the student pages to guide discussions among students about HIV and prejudice, the law, and social issues. Allow students to form their own opinions based on facts.

Part A: HIV and Prejudice

Instruct students to write a description of a "typical" HIV-infected individual. When the descriptions are complete, have students share their thoughts. Challenge the class to uncover the facts, generalities, misconceptions, and prejudices upon which the descriptions are based. Expand the concept of prejudice to include acts that occur in the school, workplace, and community. Explore how prejudice may be "fueled" by misconceptions and ignorance.



Video Connection:
Discuss the HIV-infected young people in the video.

What do students think about them?

Do they seem "typical"?

Part B: HIV and the Law

Present the following scenarios to your class. Encourage student discussion and debate.

1. A patient will soon be operated on by a surgeon. Prior to the operation, the patient overhears that the surgeon recently was tested for HIV. Should the patient have the legal right to know the physician's HIV status? Should the right of privacy protect the physician's HIV status?
2. While being arrested for disorderly conduct, a woman scratches and spits on a police officer. In custody, she tests positive for the HIV virus. Should she be charged with attempted murder? Would her prior awareness of her HIV status affect her case?
3. A sport's team physician learns that one of her players is infected with HIV. Does she have the right to have the player removed from the team? Should she be allowed to inform the other players of the HIV status? Should the type of sport affect her decision?

Part C: Personal and Social Responsibilities

Draw three columns on the chalkboard. Label them "self," "family," and "community." Have students fill in the columns with behaviors and hygiene that maintains the wellness of each group. Encourage them to include measures that address HIV disease.

The Future of the Pandemic

OUTSIDE THE LAB

How would you feel if a member of your family were sick with AIDS and there was no medical help available? Worldwide, most people infected with HIV live in poor countries. Sick people there often do not have access to modern medical facilities that are stocked with the latest therapeutic drugs. These people may die of AIDS without ever seeing a doctor, or knowing why they were sick.

Counting Problems

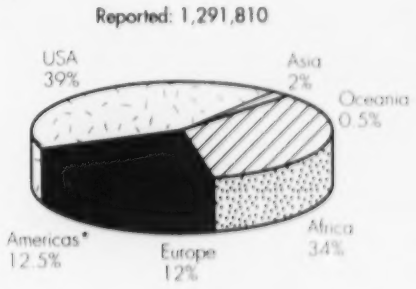
Look at the two pie charts at right. The top chart illustrates the numbers of AIDS cases that were reported between the late 1970s through 1995. Of the regions identified, the United States reported the greatest percentage of the total AIDS cases. Now look at the bottom chart. When unreported AIDS cases are included, the statistics shift dramatically. From this graph, one can see that the majority of global AIDS cases (although mostly unreported) are in people who live in regions of Africa.

In affluent countries, such as the United States, a person sick with HIV disease is more likely to seek medical attention at a hospital (because hospitals are available). Trained doctors will examine the patient's symptoms, test for HIV infection, and make a diagnosis. This diagnosis is reported to a national agency like the Centers for Disease Control and Prevention, which keeps an official record of HIV cases in the United States. However, in a developing country where little medical attention is available, the HIV cases may not be counted.

Numbers of HIV infections also are difficult to count accurately. As you know, an HIV-infected person can live for several years without having serious symptoms of infection. During this period, that person will probably not get tested for HIV. Therefore, the reported cases of HIV infection are only a fraction of the actual infections. According to some epidemiologists, of the estimated 780,000 people infected with HIV in the United States, three-quarters of them may not know that they are infected.

Accurate numbers of HIV infections help scientists track the spread of disease. Somehow the unreported HIV cases must be considered and added to the statistics. Based on information coming from many different countries, scientists make a best guess, or an estimate, of worldwide HIV infections and AIDS cases.

Total number of AIDS cases from late 1970s/early 1980s until late 1995
Data from UNAIDS



Not including USA
**Adjusted following review of global estimates*

Estimated number of persons living with HIV/AIDS

Global total 21.8 million HIV-infected people

In the United States, the number of new cases seems to be leveling off. However, the new infections are occurring through sexual transmission and sharing of infected needles. AIDS-related illnesses have become the leading cause of death in young men and women.

Globally the view is more somber. According to United Nations' estimates, about 22 million people are infected worldwide. Most of these people reside in Central and West Africa. The map above illustrates the global distribution of HIV infections which was presented at the XI International Conference on AIDS in 1996.

Although the global spread of HIV may not be encouraging, the research is. In many laboratories, new therapies and drugs are being designed and tested. Recently, promising research results have renewed hopes for a successful treatment for HIV and AIDS. How much longer will it take? No one can say with certainty. For now, the best weapon against the spread of the disease is education.

Questions

1. Describe two factors that account for disparities in HIV/AIDS statistics.

2. Using the world map graphic, determine each region's estimated percentage of global HIV infection.

North America _____
Caribbean _____
Latin America _____
Western Europe _____
Eastern Europe _____
North Africa and Middle East _____
Sub-Saharan Africa _____
Asia _____
North and South Pacific _____

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The Future of the Pandemic

Objective

Students will learn about difficulties in compiling HIV statistics and gain a global perspective of the pandemic.

Teacher Notes

Have students compare and contrast the two graphics (pie charts and world map). Review with your students the difference between the information displayed:

(a) reported AIDS cases and estimated AIDS cases;

(b) current estimates of HIV infection.

Explain that AIDS is only the last stage of HIV infection. Also, make sure that students understand that **estimates of AIDS deaths** (as reported in the video) **are different from current HIV infection estimates**, even though most HIV infected people will eventually die of AIDS. The estimates on page 166 do not include all the people who have already died of AIDS.

The Centers for Disease Control (National Center for HIV, STD, and TB Prevention) and the World Health Organization (UNAIDS - Joint Programme of HIV/AIDS) maintain very useful Internet sites for statistics and other HIV information. (See page 170.)

A GLOBAL PERSPECTIVE

In order to understand the global impact of HIV, students should have some basic geographical knowledge of the world. Many current atlases of the world include standard of living charts for each country. Some students may not be aware of the significant differences between wealthy and poor nations. For example, many Americans take modern medical care for granted. Have students discuss what it would be like to live in a country where few modern hospitals existed. Students could do a report on how HIV is affecting one particular nation.

Answers to Student Questions

1. Disparities associated with lack of diagnoses and reporting in developing countries; the long period during which an HIV-infected person may not be aware of his or her status.
2. Percentages of estimated HIV infections worldwide by geographic area:

North America	3.6%
Caribbean	1.2%
Latin America	6%
Western Europe	2.2%
Eastern Europe	.1%
North Africa and Middle East	.9%
Sub-Saharan Africa	64%
Asia	22%
North and South Pacific	.2%

Selected Bibliography

The books and journals listed below may be useful for further study or background reading. Numerous journal articles, Internet sites, books, and textbooks were consulted in the preparation of this book; this list is a selected sample of the available resources on HIV and AIDS.

Books on HIV/AIDS

Alali, A. Odasuo, ed. *HIV and AIDS in the Public Schools*. Jefferson, NC: McFarland & Company, Inc., 1995.

Appleman, M. Michael, and DellaCorte, Christian. *AIDS, Lessons From the First Decade*. Dubuque, IA: Kendall/Hunt Publishing Co., 1992.

DiClemente, Ralph, and Peterson, John L. *Preventing AIDS: Theories and Methods of Behavioral Interventions*. New York: Plenum Press, 1994.

Douglas, Paul Harding, and Pinsky, Laura. *Essential AIDS Fact Book*. New York: Pocket Books, 1996.

Fan, Hung, Conner, Ross F., and Villareal, Luis P. *The Biology of AIDS*. 3d ed. Boston: Jones and Bartlett Publishers, 1994.

Karn, Johnathan, ed. *HIV: A Practical Approach. Vol. 1, Virology and Immunology*. Oxford: IRL Press at Oxford UP, 1995.

———. *HIV: A Practical Approach. Vol. 2, Biochemistry, Molecular Biology, and Drug Discovery*. Oxford: IRL Press at Oxford UP, 1995.

Silin, Jonathan. *Sex, Death, and the Education of Children*. New York: Teachers College Press, Columbia University, 1995.

Stine, Gerald J. *AIDS Update 1996*. (Annual) Englewood Cliffs, NJ: Prentice Hall, 1995.

Biology/Medical Textbooks

For in-depth background on cell biology, physiology, immunology, and virology

Campbell, Neil A. *Biology*. 4th ed. Redwood City, CA: Benjamin/Cummings Publishing Co., Inc., 1996

Guyton, Arthur, and Hall, John E. *Textbook of Medical Physiology*. 9th ed. Philadelphia: W.B. Saunders Company, 1995.

Levy, Jay, Fraenkel-Conrat, Heinz, and Owens, Robert A. *Virology*. 3d ed. Englewood Cliffs, NJ: Prentice Hall, 1994.

Roitt, Ivan M., Male, David K., and Brostoff, Johnathan. *Immunology*. 4th ed. London: Times Mirror International Publishers Ltd., 1996.

Journals

Science, *Science News*, *Scientific American*, *Trends in Immunology*, *Trends in Biochemistry*, and the *Current Topics* series regularly publish updates on HIV and AIDS research.

Internet Resources

The subject of HIV/AIDS is covered very well on the World Wide Web. Use the following sites as stepping off points for keeping abreast of changes in research and social impacts of HIV infection and AIDS.

United States Government and International Organizations

Centers for Disease Control and Prevention Sites

http://www.cdc.gov/
Main CDC site

Division of HIV/AIDS Prevention
http://www.cdc.gov/nchstp/hiv_aids/dhap.htm
Excellent site with fact sheets, statistics, and clearly written summaries

Morbidity and Mortality Weekly Report
http://www.cdc.gov/epo/mmwr/mmwr.html
CDC publication on-line

National Institutes of Health Sites

http://www.nih.gov/index.html
Main NIH site

National Institute of Allergy and Infectious Diseases (NIAID)
http://www.niaid.nih.gov/research/divisions.htm
Listing of research divisions with links to Division of AIDS resources

AIDS Information Gopher Menu
gopher://odie.niaid.nih.gov:70/11/aids
Excellent site with links to many resources

World Health Organization Sites

http://www.who.ch/
Main WHO site

UNAIDS - The Joint United Nations Programme on HIV/AIDS
http://gpawww.who.ch/
Global perspective on the HIV/AIDS pandemic; excellent statistics and reports

Other Organizations

Abbott Laboratories
http://www.abbott.com/

AIDS Virtual Library
http://planetq.com/aidsvl/index.html
Social, political, and medical topics

The Body
http://www.thebody.com/
A multimedia AIDS and HIV information resource

The Red Ribbon Net
http://www.redribbon.com/
Information and research database, pharmaceutical company links, and AIDS service organizations

Science magazine on-line
http://www.sciencemag.org/science/home/
Global weekly of research; newest updates on HIV appear regularly

Scientific American on-line
http://www.sciam.com/
Includes excellent graphics

Unofficial Sites of Interest

Dr. Chin's Homepage
http://www.aimnet.com/~jchin/homepage.htm
Dr. James Chin is an epidemiologist who has linked together current reports on HIV/AIDS.

Marty Howard's HIV/AIDS Homepage
http://www.smartlink.net/~martinjh/
A personal touch: Marty Howard is HIV positive, and is married to a teacher. His homepage connects to numerous HIV/AIDS sites.

About the Author

Michael Anthony DiSpezio has devoted his active and diverse professional life to science education. With a renaissance approach to educational projects, he has taught, written books, developed curriculum, conducted workshops, and produced videos.

Michael received an M.A. in Biology from Boston University, and for six summers was a research assistant to Nobel laureate Albert Szent-Gyorgyi. He taught a variety of middle and high school science subjects for eight years, and taught classes at Boston University and Boston University School of Nursing.

He is co-author of eighteen elementary, middle, and high school science textbooks and is the writer of several trade books on optical illusions and critical thinking puzzles. He has written and developed curriculum for dozens of science publications, including the JASON Project. He has been published in science education journals, including NSTA's *Science Scope*, *Science and Children*, *The Science Teacher*, and *Quantum*. He also develops curriculum and writes classroom guides for *Discover* magazine and for the television show, "Scientific American Frontiers."

Involved in many television and video projects as a writer, reviewer and producer, he has worked as an educational advisor in the Middle East. His talents also led him to design and help construct interactive museum space at the Cape Cod Children's Museum.

A dynamic presenter, he regularly conducts workshops at NSTA conventions and other organizational meetings around the United States.

Michael lives in North Falmouth, Massachusetts with his wife, Susan Ketchen, and his son, Anthony.

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